The Journal of the American Medical Profession

MEDICAL TIMES

Early Rising of Puerperae
Improving Peripheral Circulation
The Sexual Offender Problem
Enterobiasis
Antispasmodic Therapy
Splenic Metaplasia
Premature Infants

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Editorials
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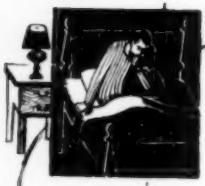

when **night cough**

produces . . . insomnia

Syrup Sedulon, a new, non-narcotic cough preparation, usually controls "night cough" which robs the patient of needed sleep. Syrup Sedulon, given in therapeutic doses, seems to act specifically on the cough reflex without interfering with heart rate or respiration. Because of its mild sedative effect, the patient sleeps well, and next day experiences no after-effects. Sedulon, the unique active ingredient, has a wide margin of safety, is well tolerated, and remarkably effective even in persistent "night cough."

HOFFMANN-LA ROCHE INC. • NUTLEY 10 • N. J.

syrup **Sedulon**®

'Roche'

Penicillin Protection by the Calendar

not by the clock

when you use

Flo-Cillin "96"

Bristol Laboratories Trademark For
CRYSTALLINE PROCAINE PENICILLIN G IN OIL
(300,000 units per cc.)
With Aluminum Monostearate, 2%

This remarkable development in repository penicillin therapy ends the need for *daily* injections. A single injection of 1 cc. produces therapeutic blood levels lasting 96 hours (4 days) in 90% of patients. A single injection *every other day* is considered adequate for most clinical purposes. Exceptionally severe conditions may require more frequent dosage.

Bristol
LABORATORIES INC.
SYRACUSE, NEW YORK

Constantly Fluid · Requires No Prolonged Shaking · Will Not Clog the Needle

for maintaining urinary alkalinity during sulfonamide therapy

One heaping teaspoonful provides:
Calcium Glycerophosphate, 1 6/10 grs. 0.10 Gm.
Magnesium Phosphate, 3½ grs. 0.22 Gm.
Calcium Phosphate, 3½ grs. 0.22 Gm.
Potassium Bicarbonate, 7 grs. 0.45 Gm.
Sodium Bicarbonate, 17 grs. 1.10 Gm.
Sodium Citrate, 48 grs. 3.11 Gm.

specify . . . 'alka-zane'*
alkaline effervescent compound

'Alka-Zane'* Alkaline Effervescent Compound gives a supply of different bases normally present in the body. The use of a variety serves to be more "natural" than administering a single alkali such as sodium bicarbonate.

'Alka-Zane' Alkaline Effervescent Compound is a pleasant and efficient agent for alkalinizing the urine; in addition, it encourages a good fluid intake. These properties make 'Alka-Zane' a very useful product during sulfonamide therapy where it is necessary to raise the pH of the urine and insure a good fluid intake to prevent crystalluria. 'Alka-Zane' Alkaline Effervescent Compound in water produces a palatable drink that makes it easy to get patients to take enough fluids.

How Supplied: 'ALKA-ZANE' Alkaline Effervescent Compound is supplied in 1 1-2 oz., 4 oz., and 8 oz. bottles.

*T. M. Reg. U. S. Pat. Off.

William R. Warner & Co., Inc. 113 West 18th Street, New York 11, N. Y.

WARNER

PROVE CAMEL MILDNESS *for Yourself!*

Test for yourself what throat specialists reported when a 30-day smoking test revealed:

"NO THROAT IRRITATION due to smoking CAMELS!"

MAKE YOUR OWN 30-DAY CAMEL MILDNESS TEST. Smoke Camels, and only Camels, for 30 days. Prove for yourself how mild Camels *are!*

Hundreds of men and women, from coast to coast, recently made a similar test. They smoked an average of one to two packs of Camels a day for 30 days. Their throats were carefully examined by throat specialists. And after a total of 2470 examinations – these throat specialists reported *"not one single case of throat irritation due to smoking Camels!"*

But prove it yourself... in your "T-Zone" (T for Taste and T for Throat).

R. J. Reynolds Tob. Co., Winston-Salem, N. C.

According to a Nationwide survey:

MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE

Doctors smoke for pleasure, too! And when three leading independent research organizations asked 113,597 doctors what cigarette they smoked, the brand named most was Camel!

Orapen-250

It is now possible to give 250,000 units of crystalline penicillin G (potassium salt) in one coated, pleasant-tasting, buffered tablet, if you specify the Schenley product. Ample evidence supports the value of the oral administration of penicillin when given in sufficiently high dosage. Clinical reports show that even serious infections due to penicillin-sensitive organisms—such as acute respiratory illness,[1,2,3,4] impetigo,[4] gonorrhea,[5] and rheumatic fever (prophylaxis)[6]—can be treated effectively by this convenient, painless method of administration.

ORAPEN IS UNIQUE
A special coating completely masks the taste of penicillin. ORAPEN is stable at ordinary room temperatures, eliminating necessity for refrigeration.

REFERENCES:

1. J. Pediat. 32:1 (1948).
2. Am. J. M. Sc. 213:513 (1947).
3. J. Pediat. 32:119 (1948).
4. New England J. Med. 236:817 (1947).
5. New York State J. Med. 48:517 (1948).
6. Lancet 1:255 (1947).

Orapen-250
Orapen-100 · Orapen-50
[PENICILLIN TABLETS SCHENLEY]

Each containing 250,000, 100,000, or 50,000 units of Penicillin Crystalline G, buffered with calcium carbonate.

ORAPEN-250:
Available in bottles of 10 and 50.
ORAPEN-100:
Available in bottles of 12 and 100.
ORAPEN-50:
Available in bottles of 12 and 100.

SCHENLEY LABORATORIES, INC.
350 FIFTH AVENUE • NEW YORK 1, NEW YORK

Contents

Contents

liver disorders

cirrhosis
fat infiltration
functional impairment
toxic hepatitis
infectious hepatitis

methischol

(pronounced meth' is kol)

A synergistic combination of METHIONINE, CHOLINE and INOSITOL in a LIVER-VITAMIN B COMPLEX BASE . . . lipotropic substances which favor the transport o fat from the liver to the fat depots of the body . . . for prophylaxis, retardation and specific therapy in reparable liver damage.

each tablespoonful or 3 capsules contain:

dl-Methionine	333 mg.
Choline	250 mg.
Inositol	166 mg.

together with the natural B complex from 12 grams of liver.

Supplied, in bottles of 100, 250, 500 and 1000 capsules and 16 oz. and gallon syrup.

advantages of **methischol**

1. three efficient lipotropic agents.
2. natural B complex from liver.
3. essential, readily utilized METHIONINE.
4. well tolerated, non-toxic, convenient.

Detailed literature and sample.

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Medical Book News

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NUMOTIZINE

THE PRESCRIPTION
CATAPLASM

...provides relief from pain and discomfort

for a period of eight hours or longer...

produces a degree of local anesthesia ...

promotes increased circulation in the area,

reducing swelling and congestion.

With Numotizine there is no necessity

for frequent changes of dressings—

no hot water bottles or electric pads.

4, 8, 15 and 30 ounce jars.

NUMOTIZINE Inc.
900 N. FRANKLIN STREET
CHICAGO 10, ILLINOIS

MEDICAL TIMES

THE JOURNAL OF THE AMERICAN MEDICAL PROFESSION

Incorporating the

LONG ISLAND MEDICAL JOURNAL

WESTERN MEDICAL TIMES

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The dihydro form of streptomycin

Dihydrostreptomycin Squibb

HYDROCHLORIDE

PERMITS HIGHER DOSAGE FOR MORE PROLONGED PERIODS

WHAT IS IT?

A potent antibiotic compound derived from streptomycin by reduction with hydrogen.

WHEN IS IT INDICATED?

Like streptomycin, as an adjunct to other measures in tuberculosis.

HOW DOES IT ACT?

The antibacterial activity of Dihydrostreptomycin usually parallels that of streptomycin in tuberculosis. Resistant strains of organisms appear to develop as rapidly as with streptomycin.

WHAT ARE ITS ADVANTAGES?

Dihydrostreptomycin is significantly less neurotoxic than streptomycin and hence can be given in larger doses and for more prolonged periods. In addition, patients showing allergic reactions to streptomycin have been able to continue with the dihydro form.

HOW IS IT ADMINISTERED?

Only intramuscularly, pending further clinical studies.

WHAT IS THE DOSAGE?

Daily doses of 2 grams of Dihydrostreptomycin Squibb may be given safely for periods equal to those in which streptomycin has been restricted to 1 gram a day, provided there is no renal dysfunction. Average dosage—1 to 2 grams daily in divided doses every 12 hours.

HOW SUPPLIED?

20 cc. vials containing the equivalent of 1 Gm. streptomycin base
50 cc. vials containing the equivalent of 5 Gm. streptomycin base

E. R. Squibb & Sons, New York 22, N. Y.

SQUIBB *a leader in antibiotic research and manufacture*

Board of Contributing Editors

A new measure for better cough control

'Elixoid'

'ELIXOID' brand Cough Syrup contains:

Ethylmorphine Hydrochloride for its highly efficient action in suppressing unproductive cough. Grain for grain, a more potent analgesic than codeine. Especially desirable where pain or night cough prevents sleep.

Sodium Citrate for its liquefying effect. Preferred over acid salts for its systemic alkalinizing properties.

Citric Acid as a buffer; for stability and full potency.

Fluidextract of Ipecac—in low, non-emetic dosage—to synergize the secretion of protective fluids.

Menthol for its cooling, soothing, analgesic effect on associated sore throat.

Aromatic Syrup, a delicious flavor to ensure acceptance by both children and adults—and just viscid enough to provide a local demulcent effect.

In each fluidounce:	
Ethylmorphine Hydrochloride	gr. ¼
Citric Acid	gr. 5
Sodium Citrate	gr. 20
Fluidextract of Ipecac	min. 2
Menthol	gr. 3/100
Aromatic Syrup	q. s.

Bottles of 1 pint

EXEMPT: 'Elixoid' Cough Syrup is an exempt preparation under Federal Narcotic Law. (Consult state and municipal laws for local status.)

DOSAGE: One teaspoonful (4 cc.) every three hours or as required. Children, according to age.

'Elixoid'

brand **COUGH SYRUP**

contains no alcohol, chloroform or barbiturates

BURROUGHS WELLCOME & CO. (U.S.A.) INC., TUCKAHOE 7, NEW YORK

NEW EFFECTIVE HEMATINIC

Laurium

provides readily available iron for the anemia patient.

Gastrointestinal symptoms are notably absent, since the source of iron in Laurium is ferrous gluconate — readily absorbed, well utilized, better tolerated.

In treatment of iron deficiency and nutritional anemias — despite the qualitative and quantitative adequacy of the iron prescribed — the conversion of iron salts to hemoglobin may be balked by absence of necessary hemopoietic adjuncts. Laurium is fortified with adjunctive hematinic principles that

promote utilization of iron
stimulate erythropoiesis
correct concomitant vitamin deficiencies

Laurium

Administration—As a dietary supplement, one or two capsules daily.

In the treatment of hypochromic or nutritional anemia, one or two capsules three times daily as required by the severity of the anemia and the response to therapy.

Laurium

Each capsule contains:

Ferrous Gluconate	280 mg.
Liver Concentrate (1:20) (Equivalent — 4 Gm. Fresh Liver)	200 mg.
Folic Acid	1 mg.
Thiamine Hydrochloride	2 mg.
Riboflavin	1 mg.
Niacinamide	10 mg.
Ascorbic Acid	15 mg.

Each capsule contains approximately 33 mg. of elemental iron—three times the Minimum Daily Adult Requirement—two times the M.D.R. for thiamine, one-half the M.D.R. for riboflavin and ascorbic acid, with 10 mg. of niacinamide. The need for folic acid in human nutrition has not been established.

Laurium: supplied in bottles of 100 capsules.

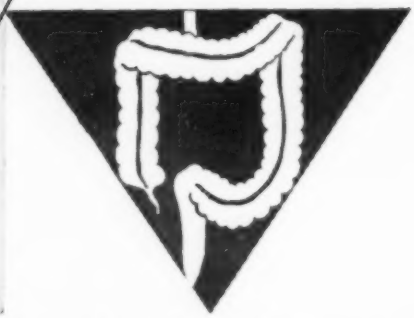
Whittier

LABORATORIES

Division Nutrition Research Laboratories

Chicago 30, Illinois

gentle bulk...



Plus proper lubrication, for effective prevention and control of chronic constipation. Konsyl, the original Plantago Ovata concentrate, establishes this therapeutic balance . . . designed particularly for those people who feel they must "take something" every day.

Konsyl is not a laxative in the usual sense of the word since it will not move the bowels of one who is constipated. But, by adding adequate bulk and lubrication, without leakage or irritation, it promotes normal peristalsis, leading to normal defecation. A rounded teaspoonful taken either before or after meals produces soft and easily-evacuated stools.

Send for a sample today—try it in your next applicable case.

SUPPLIED IN 6 and 12 OZ. CANS

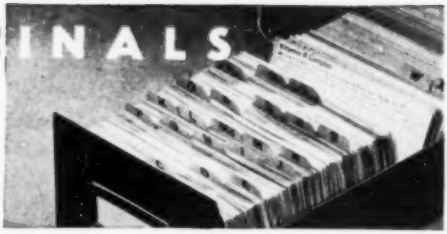
KONSYL

in chronic constipation

Burton, Parsons & Company

1515 U STREET, N. W. · WASHINGTON 9, D. C.

Modern MEDICINALS



Physicians will find that these brief resumes of essential information relative to the newer medicinals are so prepared that they may be removed and pasted on standard 3x5" file cards, and filed as illustrated in the adjoining picture, for ready reference.

Penicillin Potassium Troches

1-49

MANUFACTURER: Abbott Laboratories, North Chicago, Ill.

INDICATIONS: Indicated as an adjunct in acute ulceromembranous gingivitis (Vincent's infection).

ACTIVE CONSTITUENTS: Each troche contains 1000 or 5000 units of crystalline penicillin G potassium incorporated in a slowly dissolving medium.

DOSAGE: The troche should be allowed to dissolve in the mouth as slowly as possible. One troche usually lasts about 20 minutes. Treatment of Vincent's infection with troches is still somewhat experimental, but the most effective action probably will be obtained by keeping a troche in the mouth constantly during waking hours and placing one between the cheek and molars before going to sleep. If systemic effect is desired, as in deep-seated infections, penicillin should be administered parenterally as well as orally.

HOW SUPPLIED: Troches containing 5000 units, in bottles of 24 and 250; 1000 units, in bottles of 24.

Mercodol

1-49

MANUFACTURER: The William S. Merrell Company, Cincinnati 15, Ohio.

INDICATIONS: For the relief of cough in acute catarrhal bronchitis, acute tracheobronchitis, allergic bronchitis, laryngitis and for simple cough due to colds.

ACTIVE CONSTITUENTS: Each 30 cc. (1 fluidounce) contains: Mercodione (dihydrocodeinone bitartrate) 10.0 mg. (1/6 gr.); Nethamine (methylethylaminophenylpropanol) hydrochloride 0.1 Gm. (1½ grs.); Sodium citrate 1.2 Gm. (18 grs.) in a palatable aromatized syrup vehicle containing thyme, tolu and menthol.

DOSAGE: Adults — one teaspoonful; children, 3 to 12 years of age, one-half to one teaspoonful; children, 1 to 3 years of age, one-fourth to one-half teaspoonful. Repeat every three hours and as needed at night.

HOW SUPPLIED: In pints and gallons.

Terpal

1-49

MANUFACTURER: Pitman-Moore Company, Indianapolis 6, Indiana.

INDICATIONS: Sedative expectorant, a palatable suspension for promoting liquefaction of bronchial secretions.

ACTIVE CONSTITUENTS: Each fluidounce represents a suspension of: Phenobarbital, 0.129 Gm.; Terpin hydrate 1.5 Gm. in an aromatized viscous diluent. Methyl parahydroxybenzoate, 0.15 per cent, is used as a preservative. Warning: May be habit forming.

DOSAGE: Adult, one teaspoonful every three hours.

HOW SUPPLIED: In pint and gallon bottles.

—Continued on page 28a

TO *Streamline"*
CREOSOTE THERAPY
Rx *Calcreose*

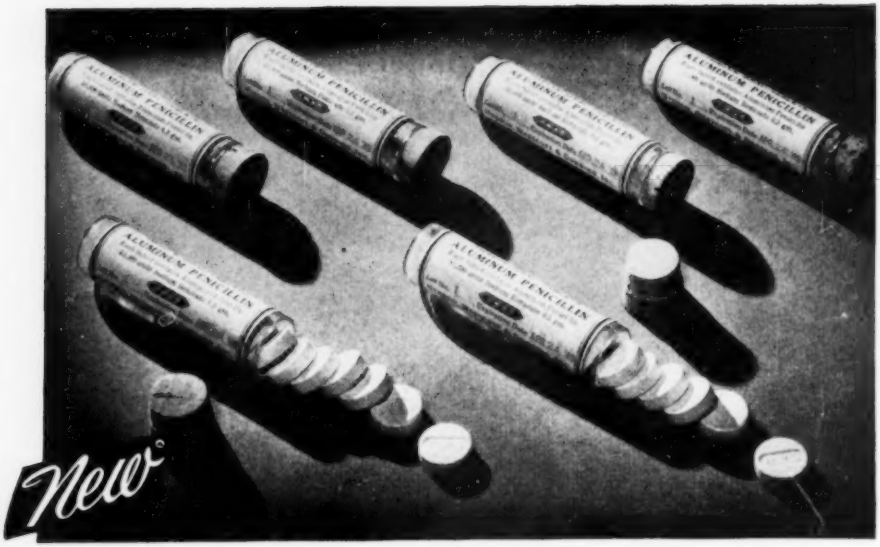
PALATABLE • WELL TOLERATED • THERAPEUTICALLY EFFECTIVE

The development of CALCREOSE (Maltbie) has, indeed, "smoothed the rough spots" in creosote therapy so frequently provocative heretofore of nausea and distress. • Moreover, CALCREOSE (calcium creosotate) exerts bactericidal and bacteriostatic action up tc *three times as great* as that of creosote. • Thus, in providing all the well-known benefits of creosote in a *pleasant* and *palatable* form, CALCREOSE proves highly effective in many bronchial and respiratory affections . . . lessening cough, diminishing expectoration, reducing its purulency and deodorizing sputum. Also it tends to stimulate the appetite and improve the patient's general condition.

AVAILABLE: As tablets (4 gr.) in bottles of 100, 500, and 1000. COMPOUND SYRUP CALCREOSE in pint or gallon bottles.

Calcreose

THE MALTBIE CHEMICAL COMPANY • NEWARK, NEW JERSEY



Aluminum PENICILLIN.*

ORAL TABLETS

Aluminum Penicillin Oral Tablets are clinically effective in the treatment of penicillin susceptible infections.

Containing the almost insoluble trivalent aluminum salt (not a mixture), they provide for maximum utilization of the dose administered.

Low solubility of Aluminum Penicillin renders it much less liable to inactivation in the stomach. Destruction in the intestinal tract is inhibited by the addition of sodium benzoate. Slow conversion to a readily absorbed form in the more alkaline conditions of the intestinal tract enhances clinical effectiveness.

Aluminum Penicillin is not toxic in doses far exceeding those used therapeutically and does not cause gastric disturbance.

Detailed information will be sent to physicians on request.

Specify Aluminum Penicillin Oral Tablets, H. W. & D.

Supplied in vials of twelve tablets each containing Aluminum Penicillin, 50,000 units, and sodium benzoate, 0.3 gram.

Oral Tablets

*Patent applied for

NOW COUNCIL ACCEPTED

HYNSON, WESTCOTT & DUNNING, INC. BALTIMORE MARYLAND

MERCODOL is more effective because it contains:

AN IMPROVED NARCOTIC *MERCODINONE* (dihydrocodeinone bitartrate)—6 times more potent (by weight) than codeine—is superior in antitussive action to both codeine and heroin, yet notably free from such side effects as nausea, constipation and retention of sputum. The cough reflex is controlled—made productive—but not completely abolished.

A SAFER BRONCHODILATOR *NETHAMINE* relaxes bronchioles to facilitate breathing and help relieve congestion—without central nervous or cardiovascular stimulation.

A BETTER EXPECTORANT *SODIUM CITRATE* stimulates flow of protective mucus, to lessen acute inflammation and to thin gummy bronchial plugs.

Trademarks "Mercodol," "Mercodinone," and "Nethamine."

Because MERCODOL *TASTES SO GOOD*, your patients—even youngsters—will not object to taking it. And because it is compatible with a wide variety of drugs used in adjunctive therapy, Mercodol makes an unusually pleasant, therapeutically active vehicle.

DOSAGE: *Adults*—1 teaspoonful; *children*—¼ to 1 teaspoonful. Repeat every three hours and as needed at night.

AN EXEMPT NARCOTIC, Mercodol is available at hospital and prescription pharmacies.

• • •

MERCODINONE TABLETS: For addition to Mercodol to increase narcotic effect, or prescribed alone for the racking coughs of severe pulmonary diseases. Soluble 5 mg. tablets in 20's and 100's.

THE WM. S. MERRELL COMPANY • CINCINNATI, U. S. A.

MERRELL 1828

To Assure Potency and Balance in Vitamin B Therapy...

KINNEY'S FORTIFIED YEAST PRODUCTS

Numerous clinical reports have indicated that in the treatment of vitamin B deficiency, optimal response is secured by giving the patient whole vitamin B complex derived from a natural source such as yeast, plus specific crystalline B factors. Precipitation of other vitamin deficiencies, often caused by single vitamin therapy, is thus avoided.[1,2]

Kinney's Fortified Yeast Products have enjoyed wide clinical application because they provide, in potent and convenient dosage forms, the entire B complex fortified by the addition of the essential crystalline B vitamins.

1. Richards, M. B.: Brit. M. J. 1: 433 (1945).
2. Elvehjem, C. A., and Krehl, W. H.: J.A.M.A. 135: 279 (1947).

FORTIFIED YEAST EXTRACT

(Kinney)

Highly concentrated aqueous extract of specially cultured yeasts with added crystalline B vitamins.

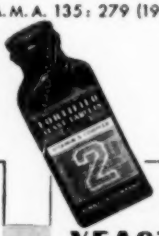
Each teaspoonful (5 cc.) contains not less than:

Thiamine Hydrochloride	2.0 mg.
Riboflavin	3.0 mg.
Niacinamide	20.0 mg.
Calcium Pantothenate .	1.0 mg.
Pyridoxine Hydrochloride	0.5 mg.

with other vitamin B factors contained in yeast extract.

DOSE: 1 teaspoonful three times daily, or as physician prescribes.

SUPPLIED: Bottles of 4 fl. oz. and 1 pint.



FORTIFIED YEAST TABLETS

(Kinney)

Concentrated tablets containing the natural vitamin B complex of 5 grains of dried brewers' yeast with added:

Thiamine Hydrochloride	2.0 mg.
Riboflavin	1.5 mg.
Niacinamide	10.0 mg.
Calcium Pantothenate .	0.5 mg.
Pyridoxine Hydrochloride	0.25 mg.

DOSE: 2 tablets two or three times daily, or as physician prescribes.

SUPPLIED: Bottles of 100 and 1,000 5-grain tablets.

Kinney®

KINNEY & COMPANY • COLUMBUS, INDIANA

MORE AND MORE....

SAFE CONTRACEPTION

Physicians prescribing KOROMEX Jelly and KOROMEX Cream where pregnancy is diagnosed as inadvisable, are recognizing the safe, non-irritating, effective qualities that are supported by a long clinical record . . . fastest spermatocidal time* . . . proper viscosity for cervical occlusion . . . the long time-period of stability . . . the effective use of spermatocidal agents in a non-irritating compound . . . the high ethical standards . . . pH consistent with the normal vagina.

ACTIVE INGREDIENTS: BORIC ACID 2.0%, OXYQUINOLIN BENZOATE 0.02% AND PHENYLMERCURIC ACETATE 0.02%, IN SUITABLE JELLY OR CREAM BASES.

*MEASURABLE UNDER THE BROWN AND GAMBLE TECHNIQUE.

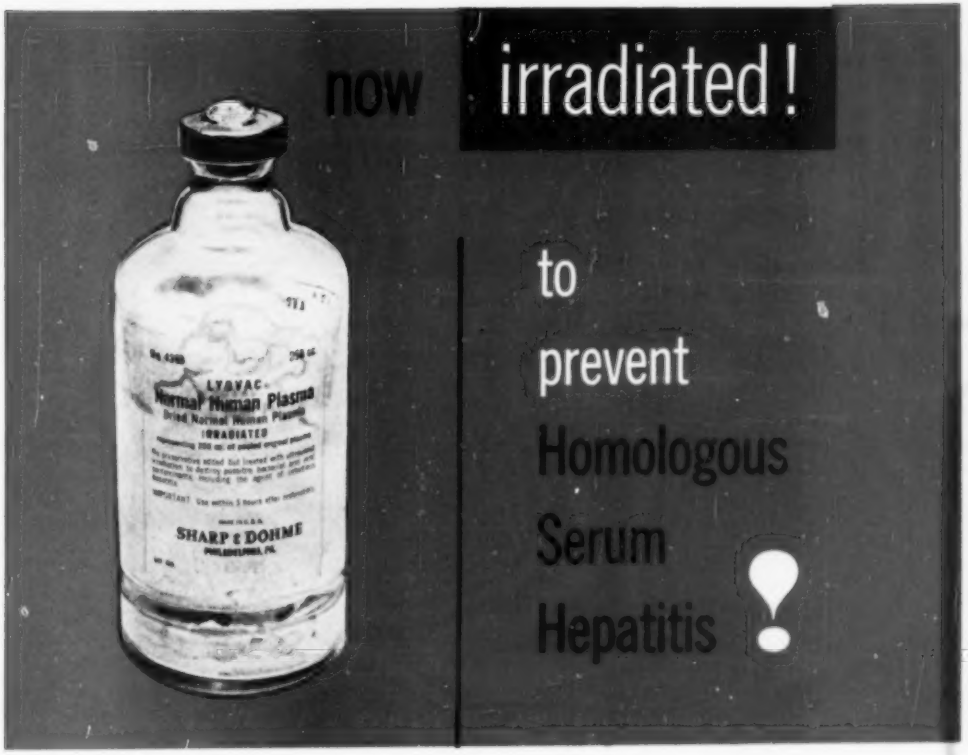
KOROMEX

TRADE MARK REGISTERED

"CHOICE OF PHYSICIANS"

HOLLAND-RANTOS COMPANY, INC., 145 HUDSON STREET, NEW YORK 13, N. Y.

MERLE L. YOUNGS, PRESIDENT



Ultraviolet irradiation of plasma destroys not only all bacteria but also any viral contaminants that might cause homologous serum hepatitis. • You may therefore administer *irradiated* LYOVAC *plasma* without danger of hepatitis. • Stable, portable LYOVAC Normal Human Plasma (*Irradiated*) is prepared from fresh, citrated, human blood of healthy donors, according to regulations of the National Institute of Health. The plasma is pooled, flash frozen, *dehydrated from the frozen state under high vacuum* (lyophile process), and sealed under vacuum. • *Blood substitute of choice for emergencies*, irradiated LYOVAC plasma is quickly restored, needs no typing or crossmatching, and each unit is osmotically equivalent to two units of whole blood. • LYOVAC Normal Human Plasma (*Irradiated*) is supplied in vacuum bottles to yield 50 cc., 250 cc. and 500 cc. of restored, *irradiated* normal plasma, or smaller quantities of *hypertonic* plasma. Sharp & Dohme, Philadelphia 1, Pa.

Lyovac®

SHARP & DOHME

Normal Human Plasma IRRADIATED

Sulfonsol 1-49

MANUFACTURER: The National Drug Co., Philadelphia 44, Pa.
INDICATIONS: In those infections caused by sulfonamide sensitive organisms.
ACTIVE CONSTITUENTS: Micro crystals of both sulfadiazine and sulfamerazine in equal parts.
DOSAGE: As indicated.
HOW SUPPLIED: In 2 fluidounce, 4 fluidounce and pint bottles.

Bacitracin 1-49

MANUFACTURER: C. S. C. Pharmaceuticals, div. of Commercial Solvents Corp., 17 East 42nd Street, New York, N. Y. and The Upjohn Co., Kalamazoo 99, Michigan.
INDICATIONS: Local application of sterile solutions of bacitracin have been found effective in treatment of furuncles, carbuncles, superficial and deep abscesses, infected wounds and ulcers, sties and impetigo. It appears to be especially advantageous for local use in that it has a wide range of activity; is highly stable; is not inactivated by bacteria, leukocytes or body secretions; is not irritating; and rarely causes allergic sensitivity.

The ointment is used in the treatment of superficial infections of the skin caused by organisms susceptible to bacitracin. Strains of streptococci and staphylococci that show resistance to penicillin are usually susceptible to bacitracin. The local application of bacitracin may be supplemented with local injections of sterile solution of bacitracin or parenteral injections of penicillin.

The ophthalmic ointment is indicated in the treatment of superficial infections of the eye involving the conjunctiva, cornea, meibomian glands and lacrimal sacs, where the infection is caused by an organism susceptible to bacitracin. For deep infections of the eye, systemic antibiotic therapy should supplement local applications.

ACTIVE CONSTITUENT: Bacitracin.
DOSAGE: For local treatment a solution containing 500 units of bacitracin per cc. is injected into the center of the lesion. In treatment of simple furuncles, injections of 0.1 to 0.5 cc. of solution daily for two to five days may be sufficient. Larger lesions such as carbuncles may require multiple injections. As injections into the lesions may give rise to pain due to an increased pressure, procaine may be injected simultaneously with the bacitracin solution. Procaine does not interfere with the antibacterial action of bacitracin.

Bacitracin solutions should be prepared by adding sterile physiological salt solution in amount sufficient to provide 500 units per cc. for wet dressings, irrigations and local injections.

The ointment is applied locally with or without a bandage, one or more times a day as required.

Application of the ophthalmic ointment is made one or more times daily as the condition indicates.

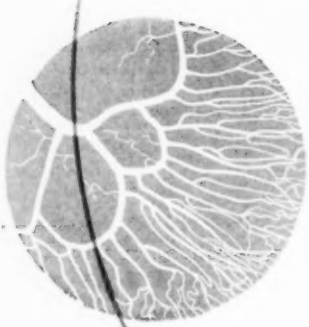
HOW SUPPLIED: C.S.C. Pharmaceuticals supplies bacitracin in 20 cc. rubber-stoppered vials containing 2,000 and 10,000 units, and in 50 cc. rubber-stoppered vials of 50,000 units. Bacitracin Ophthalmic Ointment-C.S.C. is available in $\frac{1}{8}$ ounce tubes; Bacitracin Ointment C.S.C. (for cutaneous application), in $\frac{1}{2}$ ounce tubes. Both ointments provide 500 units of Bacitracin per gram. The Upjohn Co. supplies Bacitracin Topical in sterile vials containing: 2,000-10,000 or 50,000 units, Baciguent, an ointment containing 500 units per Gm. in $\frac{1}{2}$ ounce tubes; and Baciguent-Ophthalmic, an ophthalmic ointment containing 500 units per Gm. in one drachm tubes.

RUTAMINAL

the protection of **RUTIN**

the action of **AMINOPHYLLINE**

the sedation of **PHENOBARBITAL**



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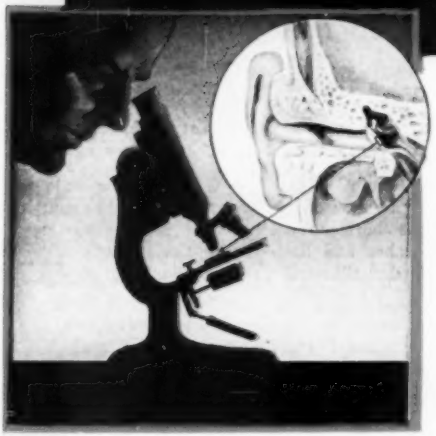

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References: 1. Karnaky, K. J.: Original gynecological and obstetrical research—sterility, endocrine and vaginal operations, M. Rec. & Ann. 35:851, 1941. 2. Smith, O. W.; Smith, G. van S., and Hurwitz, D.: Increased excretion of pregnanediol in pregnancy from diethylstilbestrol with special reference to the prevention of late pregnancy accidents, Am. J. Obst. & Gynec. 51:411, 1946. 3. Meaker, S. R.: A working classification of the causes of abortion, J.A.M.A. 123:680, 1943. 4. Rosenblum, G., and Melinkoff, E.: Preservation of the threatened pregnancy with particular references to the use of diethylstilbestrol, West. J. Surg. Obst. & Gynec. 55:597, 1947.

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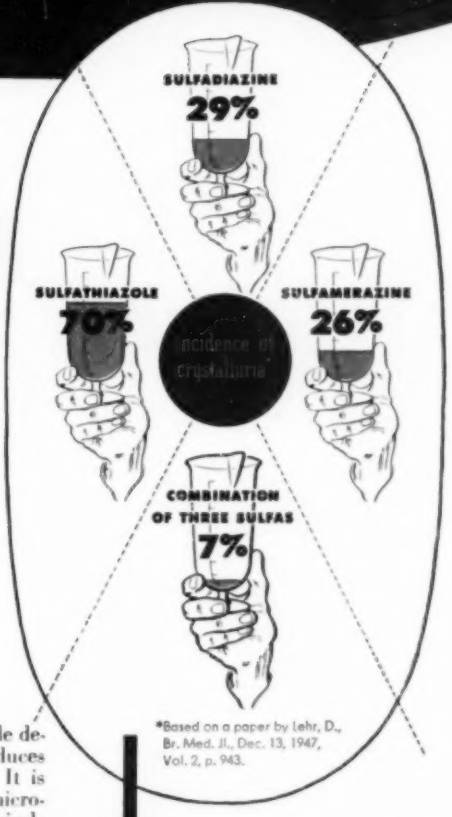

*Based on a paper by Lehr, D., Br. Med. Jl., Dec. 13, 1947, Vol. 2, p. 943.

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1. Hagerman, G.: Nord. Med., 22:1223 (1944).
2. Herlitz, S.: Nord. Med., 27:1226 (1944).
3. Lehr, D.: Proc. Soc. Exper. Biol. & Med., 58:11-14 (Jan.) 1945.
4. Lehr, D.: J. Urol., 55:546-66 (May) 1946.
5. Lehr, D.: J. Ped., 29:275-85 (Sept.) 1946.

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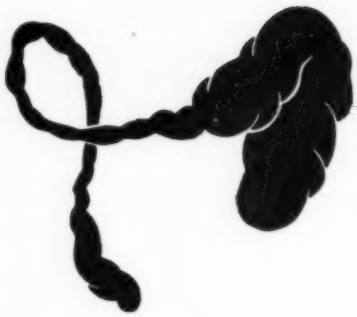
—Monat, H. A.: Constipation, Rev. Gastroenterol., *15*:242-244 (Mar.) 1948.



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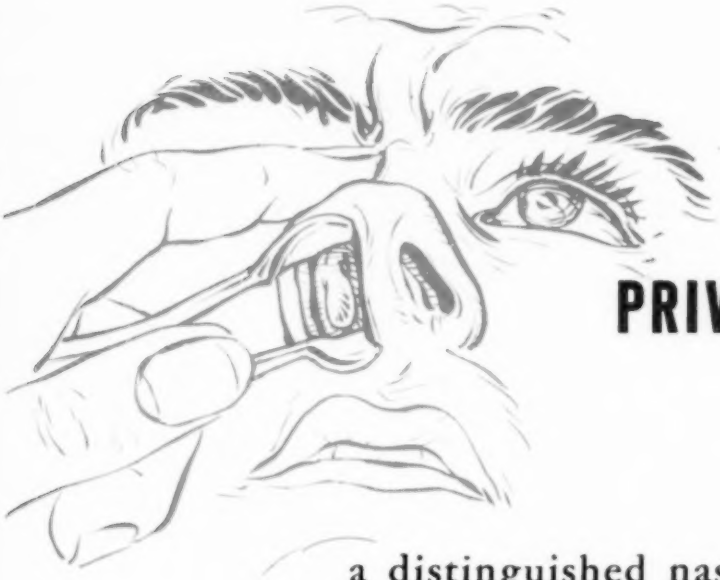

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References: (1) Lewey and Shay, Dietotherapy, Philadelphia, W. B. Saunders & Co., 1945, p. 850.

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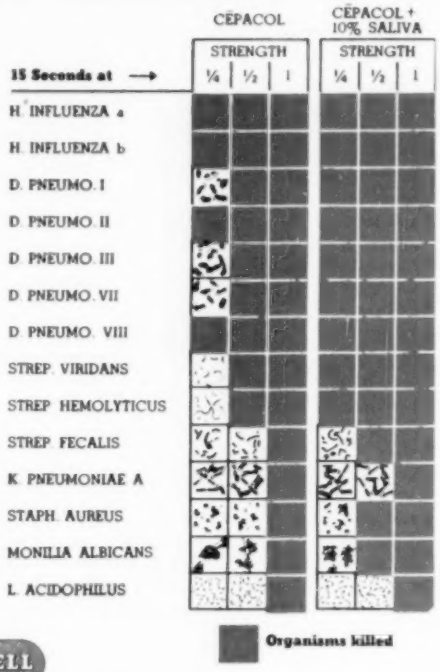

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Early Rising of Puerperae

George S. Atkinson, M.D., A.I.C.S.

Florence, Colorado

The question of early ambulation after childbirth has been discussed many times lately, but obstetrical interest on this subject goes back as far as 1899 (Kuestner). The recent revival of this interest began with Collazo (1), who in 1932 published his observations of 405 cases. His experiments were carried out on primiparae and multiparae who were in good health. The author did not observe a single case of thrombosis in his material. The percentage of retroposition of the uterus was only 1.38.

C. Stanca (2) in 1940 gives the following contraindications for early rising after childbirth: (1) Prolonged labor, (2) Elevation of temperature during the first days after delivery, (3) Extensive injury of vagina or perineum during delivery, (4) Instrumental intervention, like forceps, (5) All acute diseases of heart and lungs, (6) Infectious diseases.

Guido Ricci and Pia C. Pedro (3) in 1941 published their experiences with 551 cases. Among these cases were twelve instrumental interventions. None of these had fever during the puerperium, and only one case had shock and postpartum hemorrhage. In cases of perineal laceration early rising was not recommended.

A. B. Hudgins (4) in 1943 published his experiences. He combined the employment of non-absorbable suture in perineal repairs with sitz baths in hypertonic salt solutions and early ambulation. His results were uniformly good. Allowing the patients up in a chair or on the side of the bed added much to their comfort. It was striking how quickly the patients overcame the postpartum shocked appearance.

From the Atkinson Clinic.

Morris L. Rotstein (5), in 1944, published his results in the *Journal of the American Medical Association;* 150 patients were chosen at random, and allowed up on their third day after delivery. Among the cases were 51 spontaneous deliveries, 85 low forceps, 8 midforceps, and 6 breech deliveries, with 117 episiotomies. In this series 9 patients, or 6 percent, had a morbid puerperium, which is well below the average morbidity of service cases (7.5%). No cases of thrombophlebitis occurred.

Gordon Rosenblum, Eugene Mellinkoff, and Harry S. Fist (6), in 1945, surveyed their experiences with 574 cases, and concluded: Delivered women can safely and advantageously get up early in the puerperium with no harmful results occurring. Bowel movement particularly is improved. The amount of nursing required is greatly reduced.

The most comprehensive study on early ambulation postpartum stems from William F. Guerriero's (7) report in 1946. He followed up 2,926 cases after birth. The potential disadvantages: Postpartum hemorrhage, excessive relaxation, uterine prolapse, and dehiscence of episiotomy were fewer than in nonambulatory patients. The advantages were beyond expectations. There was a complete absence of bladder and bowel disturbances, phlebothrombosis and thrombophlebitis.

Arthur C. King (8) in 1946 reported similar findings. His series consisted of 221 women. His contraindications to early rising included the loss of 500 cc. of blood, and any unusual circumstances of labor. The use of episiotomy was not a contraindication. No harmful effects were noted as long as five months postpartum.

Six weeks after delivery 26 percent had a third degree retroversion, which compares favorably with the 40 percent of women ordinarily conceded to have retroversion at the six weeks' visit.

Clarence B. Warrenburg (9) reported his findings in 1947. He permitted his 200 patients to get out of bed and use the toilet as early as 24 hours after childbirth. In no case did a breakdown of episiotomy occur. He discharged his patients from the hospital on the fifth day.

E. Cullen Bryant (10) in 1947 published his experiences with 250 unselected cases. A study of these cases showed that early risers have a more comfortable and rapid convalescence, require less rectal treatment and medication, need less nursing care, have a much more rapid return to normal body function, a better morale, suffer no deleterious effects or delay in the healing of the perineum, have a lower incidence of retroversion, fewer complications, less postoperative invalidism and need less home convalescence.

The writer would like to report his findings in fifty cases in a general obstetrical practice, chosen at random, and allowed up the day of delivery. The following contraindications were considered deterrent to early rising: (1) Hemorrhage, (2) Severe cardiac disease, (3) Thrombophlebitis, (4) Dystocia of a complicated nature.

TABLE I Statistics

Total number of cases in series	50
Early risers	50
Vaginal deliveries	46
Spontaneous	37
Low forceps	8
Breech extractions	1
Episiotomies performed	19
Laceration repair	6
Cesarean sections	4

TABLE II Bladder Function

Number studied	50
Number requiring catherization	8
Number not requiring catherization	42
Voiding complete after first postpartum day	50

TABLE III Cesarean sections

Number in series	4
Morbidity	**0**

TABLE IV Total days hospitalization

Early risers	
Vaginal deliveries	46
Average number days hospitalization per patient	5
Cesarean sections	4
Average number days hospitalization per patient	6

TABLE V Postpartum routine

1. Frequent moving in bed immediately after delivery.
2. Patients out of bed one to four times first 24 hours, and at will thereafter.
3. Ergotrate 1/320 gr. p.c. for three days.
4. Nembutal ½ gr. and acid acetylsalicylic 5 grs. as needed for after pains.
5. Catherization of patient every ten hours if unable to void.
6. Soft diet same or next day.
7. Soapsuds enema on third day, if patient has had no bowel movement.
8. Petrolagar, plain, oz. 1, given second night if needed.
9. Perineal irrigations with ½ percent lysol solution as required.

TABLE VI Miscellaneous observations

Lochia	
Normal	47
Excessive	3
Perineal healing	
Good	22
Fair	**2**
Poor	1
Abdominal wound healing	
Good	4
Involution of uterus	
Good	**47**
Fair	2
Poor	1
Bowel function	
Moved spontaneously	5
Enema required	45
Number of breast babies	
Primiparae	5
Multiparae	15
Multiparae in series	28
Primiparae in series	22
Excessive bleeding during first postpartum month	0

Comments

1. It is evident, from the presented series of early ambulation following childbirth, that the incidence of complications is below expectations. This corroborates the previous findings of other authors.

2. Early rising after childbirth is a highly recommended postpartum procedure.

—Concluded on page 44

Study of Premature Infants in North Country Community Hospital 1944-1948

Mildred Wicker Jackson, M.D.
Oyster Bay, New York

The care of the premature child, and its results, is a problem which is always with us and a curiosity to determine how the care of these children, in a small hospital, had succeeded, and how it compared with care given in other parts of the country, prompted this paper.

The years of 1944-'45-'46-'47 were studied. During these years there were 3,060 babies born in this hospital (North Country Community Hospital) of which 99 were premature. In defining prematurity an upper limit of 5½ pounds was set which is in conformity with the concepts of the American Academy of Pediatrics. This has excluded a group of cases of 8 months gestation weighing more than 5½ pounds and has included multiple births of 9 months gestation.

The obstetrical patients were both private and service, a great majority being private. Thirty-one physicians were involved in the care of these cases.

The premature nursery was a small room, near the delivery room, equipped with four Davidson incubators. As soon as a premature birth was expected the nursery was notified, the heat turned on in the incubator and oxygen tested. The babies were carried to the nursery and placed in the incubator. Oxygen was used routinely and carbogen for cases having respiratory difficulty. Oxygen concentrations were kept at 60-65 per cent, humidity at 60-65 per cent and temperature at 80-85 degrees for the first hours and varied thereafter as ordered by the physician. The nursery was supervised, except for the last five months of this period, by a specially trained, experienced and capable nurse who had an especial interest in prematures. She had on her staff some registered nurses and some trained baby nurses. A premature was a challenge to them all and their attitude was that nothing was impossible. Without doubt their interest, patience and skill added greatly to the results obtained.

The babies were gavaged by registered nurses when they were unable to suck or bottle feeding was found to be too tiring.

The results of this care can be tabulated as follows:

*Read before the Scientific Section of the Associated Physicians of Long Island held in the North Country Community Hospital at Glen Cove, N. Y., June 15, 1948.

TABLE I

Number of births	Number died	Number lived	Total mortality	Survived %
99	26	73	26.2	73.8

TABLE II

	Lived	Died	Total	Died (%)	Survived (%)
Under 2 lbs.	0	10	10	100%	0
2-3 lbs.	3	8	11	73%	27%
3-4 lbs.	10	2	12	17%	83%
4-5 lbs.	27	5	32	15%	85%
5-5½ lbs.	33	0	33	0	100%

TABLE III

	Number lived	Number died	Total	Mortality %	Survival %
Male	33	15	48	31%	69%
Female	40	11	51	21%	79%

TABLE IV

Month of gestation	5 mo.	6 mo.	7 mo.	8 mo.
Number died	7	9	4	6
Number lived	0	2	22	44

It is interesting to note that none of the babies weighing less than two pounds lived. From two to three pounds 73 per cent died while in the three to four pound group 17 per cent died and 83 per cent lived. The four to five pound figure of survival which was 85 per cent was only slightly higher than in the previous group although the total number of cases was appreciably higher, twenty-seven as compared to ten.

The greatest number of babies who lived fell, as one might expect, in the five to five and one-half pound group, 33, and in this group there were no deaths. This is undoubtedly due to the small number of cases.

The females in this series slightly exceeds the males and their rate of survival was higher.

In attempting to analyze these figures in relation to the month of gestation it was found that the figures given were in most cases relative and in a few cases were not obtained. Those analyzed are as follows:

In this series no five month baby lived and only two of a six month period lived. Twenty-two babies falling in the seven month group lived and four died while forty-four in the eight month classification lived and six died—16 per cent mortality in the seven months group as compared to a 12 per cent mortality in the eight months group.

In reviewing the twenty-six cases who died, from point of time, twenty-two died under twenty-four hours and the other four lived over four days.

The most constant comment made on the cases who died in under twenty-four hours, was one of respiratory difficulty, irregularity and failure.

The four cases who lived longer were:

1. A case weighing 2 lbs., 3 oz. who died on the sixth day of pulmonary atelectasis and bronchopneumonia.
2. A 4 lb., 4 oz. baby who died on the sixteenth day and an autopsy revealed a peritonitis.
3. A 1 lb., 13 oz. baby who lived two months and died weighing 3 lbs., 8 oz. after repeated attacks of cyanosis.
4. A 4 lb., 15 oz. baby who died on the tenth day. This child had a tracheobronchial fistula. Gastrostomy was done. Autopsy revealed bronchial pneumonia and multiple abscesses of lung.

The causes of death in addition to prematurity which were determined in the 22 cases which died in under twenty-four hours were malformations 4, atelectasis 3, subarachnoid hemorrhage 1.

To return to the group who lived, nothing was given by mouth for the first twelve hours; 5 per cent Beta Lactose was started at the discretion of the physician

TABLE V

	Breast milk alone	Breast milk plus evaporated milk plus water plus carbohydrate	Breast milk plus evaporated milk plus Alacta	Evaporated milk plus water plus Dextri-Maltose alone
Number of cases	19	15	16	18

TABLE VI

Philadelphia Total mortality %	Houston Total mortality %	Glen Cove Total mortality %
32% (1941-1945)	22% (1944) No cases over 5 lbs. included	26% (1944-1948)

TABLE VII

Per cent of Survival	Philadelphia*	Houston	Glen Cove
Under 2 lbs.	2%	0	0
2-3 lbs.	26%	26%	27%
3-4 lbs.	46%	72%	83%
4-5 lbs.	81%	94%	85%
5-5½ lbs.	91%	....	100%

*Based on figures for 15 years 1930 to 1945.

from twelve hours on. This was given by dropper and bottle if the size and strength of the child warranted it and by gavage if it did not. Every effort was made to obtain breast milk for the smaller babies and combinations of breast milk and formulas were given as the babies grew. In the cases analyzed the following results were found:

Feeding Methods

of the 68 cases analyzed 50 had breast milk alone or in combination or succession with other foods.

Vitamins were added to the formulas in twenty-five cases.

For comparison Tyson's (1) statistics from the Philadelphia Lying-In, a branch of the Pennsylvania Hospital, and Bloxsom's (2) figures from the St. Joseph's Maternity Hospital in Houston, Texas, were used.

Dr. Powers (3) of New Haven quotes Dr. Ethel Dunham (from work sponsored by the Children's Bureau) for the United States that "under good conditions of care the prognosis for survival of premature infants in the three higher birth weight groups may be assessed as follows:

2,001-2,500 gms. (4.4 to 5.5. lbs.) Excellent. At least 93 per cent should survive. 1,501-2,000 gms. (3.3 to 4.4 lbs.) Good. At least 82 per cent should survive. 1,000-1,500 gms. (2.2 to 3.3 lbs.) Fair. At least 50 per cent should survive."

Summary

Ninety-nine premature infants were born in a general hospital over a period of four years. They were cared for by a group of thirty-one different physicians. A premature nursery with four Davidson incubators was used and oxygen given all cases. Experienced, interested, specially trained supervision and nursing were contributory factors. Twenty-six babies died, seventy-three lived. The greatest increase in the percentage who lived occurred in the 3-4 pound group, 83 per cent surviving as compared to 27 per cent in the 2-3 pound group.

The greatest number of births occurred in the 8th month of gestation, 46—2 died, 44 lived, as compared to 26 in the 7th month, 4 of whom died and 22 lived.

Feeding was started after twelve hours. Beta Lactose given first and breast milk and combinations of evaporated milk, water, carbohydrates and Alacta added.

Conclusion

The occurrence and survival of premature infants in a small community hospital has been studied and found to be comparable to similar figures in large, well organized hospitals and meets the standards set by the Children's Bureau.

References

1. Tyson, R. M.: *The Journal of Pediatrics, 28*:648 (June) 1946.
2. Bloxsom, A.: *The Journal of Pediatrics, 28*:418 (April) 1946.
3. Powers, G. F.: *Pediatrics, 1*:145 (Feb.) 1948.

SPECIAL ARTICLE

Brucellosis

This summarization attempts to cover all of the known therapeutic information on the subject and is designed as a time-saving refresher for the busy practitioner.

Reprints available*

Brucellosis, also known as undulant fever, Malta fever, Mediterranean fever, goat fever, dust fever, Neapolitan fever, Cyprus fever, Danube fever, contagious abortion, Bang's disease and others, until about 20 years ago, was relatively rare in the United States. Today it has assumed, in the field of infections, a position of importance exceeded only by tuberculosis, syphilis and gonorrhea. Although it is considered endemic, it is difficult to estimate accurately the number of active cases because of the vague symptomatology and imperfect diagnostic technics. However, in 1947 it was estimated that there are at least 55,000 active cases.[1-3] It is possible that this figure may be far too low.

History

As early as 1814 there appeared in the literature a description of a disease then known as bilious remittent fever of the Mediterranean. A differential diagnosis between this condition and malaria was based upon the fact that malaria responded to bark infusions whereas this fever did not.[4] In 1859 an organism was isolated from the spleen of patients who had died of a disease known as Mediterranean or gastric fever.[5] In 1892 the causative organism was named the *Streptococcus melitensis*.[6] Another worker, after isolating a coccoid organism from the spleen in 1887, studied it further and in 1893 named it *Micrococcus melitensis*.[7, 8] The disease was transmitted to monkeys by means of a culture.

Later the name of this organism was changed to *Bacillus melitensis* or *Bacterium melitense*. A similar organism, found to be the cause of contagious abortion in cattle, was isolated in 1897 and named *Bacillus abortus*.[9] The relationship of these organisms was not recognized until a member of the United States Public Health Service showed that the organisms were simply different strains of the same coccoid form and that the names mentioned previously applied to one disease.[10] Because of their resemblance microscopically it was suggested that the organisms be given the generic term *Bacterium*.[11] This genus was already over burdened so that it was recommended that a more suitable generic name would be *Brucella*.[12] This therefore was approved and accepted.

Hosts

A member of the Mediterranean Fever Commission discovered in 1905 that the chief host of *Br. melitensis* is the milch goat.[12] In the goat the organism more or less localizes in the udder, spleen and lymph nodes resulting in an interstitial mastitis and splenic lymphadenitis. Since this time the organism also has been isolated from the milk of infected cows in the United States, France and Italy as well as from aborted fetuses of sheep and goats in France, Italy and Argentina.[13]

Br. abortus appears to use the udder of the cow as a reservoir resulting in acute diffuse and chronic productive inflamma-

* From the Editorial Research Department of the MEDICAL TIMES, 67 Wall Street, New York 5, N. Y. Permanent library binders, sufficient to hold 24 different "refresher" reprints, sent postpaid $2.50.

***Fig. 1. Bull with testicle infected with* B. abortus.**

tion of the maternal and fetal placentae, fetal pneumonia and chronic interstitial mastitis. There may occur also an inflammatory process in the uterus and Fallopian tubes of heifers and mature cows or in the testes of the bull. This organism has been found in animals all over the world and has been recovered from naturally infected humans, horses, fowl, dogs, sheep, wild deer, and wild buffalo.[13]

Br. suis is another closely related organism and has been isolated from hogs in the United States, Hungary, Denmark, Switzerland, Brazil, Argentina, and Japan. It has been found in infected humans, horses, fowl, cows, and dogs.[13]

The condition brought about by these organisms in humans was first found in goat herders and individuals who drank goat milk. Veterinarians were next observed to contract it and then, finally, the general population.[14]

Incidence

Although the first authentic case of brucellosis was reported in the United States in 1905 [15] its endemic nature was not revealed until 1911 when it was found to be prevalent in Southwestern Texas. Goat's milk was the cause. Further study revealed that it had been occurring for some years.[15, 16] Because of the difficulty of diagnosis it is believed to have been in existence for many more years than are reported. The number of reported cases has been increasing annually but it is thought that the true incidence has decreased rather than increased. The disease has been found more commonly in rural areas than in urban areas because of the increased possibility of contact with infected animals or the use of unpasteurized dairy products in the former areas. Urban areas frequently show an increased incidence following the summer vacation period.[17, 18]

Certain states have had incidence rates greater than those in other regions which is not explained by a larger rural population since other states with higher proportions of rural residents had low incidence rates. A high incidence of the infection in cattle is not responsible either, therefore it is believed to vary directly with the size of the hog and goat-raising industry in the area.

Brucellosis may occur at all ages, except during the nursing period of infancy, but it occurs more frequently in young adult males probably because so many of the occupational groups which it affects are farm workers and packing-house employees among whom the incidence is high. This would suggest therefore that there is a risk in those occupations in which livestock and fresh meat are handled.

In proportion to the wide distribution and high prevalence of *Brucella* infection in cattle the incidence of infections from *Br. abortus* is low. This type of infection

is generally mild but the caprine and porcine types are more pathogenic to humans.[19] However, the total number of cases appears to be increasing and there is substantial evidence to indicate that swine are responsible for 70 to 93 per cent of the human infection.[20]

Etiology

Brucellosis is an infectious disease of acute and chronic nature varying considerably in its symptoms and in its duration. It is caused by a pleomorphic organism which sometimes appears as a coccus and sometimes as a small bacillus. The organism is minute, nonmotile and Gram-negative and when first isolated grows very slowly on a special culture medium. Sugars are not fermented by it and it strongly resists drying. The three varieties *Brucella melitensis*, *Brucella abortus* and *Brucella suis* are also known respectively as *Brucella abortus caprinus* (goat), *Brucella bovinus* (cattle) and *Brucella porcinus* (hog). They may be differentiated by means of hydrogen sulfide metabolism, the bacteriostatic action of dyes, glucose utilization, reduction of nitrates and nitrites, measurement of time potential in an oxidation-reduction system, chemical differences in the cells, and immunologic reactions.[13, 14]

Pathology

A pathological examination of a patient with brucellosis reveals the usual changes which are observed in any general infection not having a specific lesion. Chiefly affected are the liver and spleen. Examination of the liver reveals small areas of focal necrosis, small foci of reticulocytes and lymphocytes, and areas of endo- and thrombophlebitis with discrete and confluent granulomata somewhat like tubercle. The spleen may be enlarged. The intestinal mucosa may exhibit small ulcers and the kidneys and lungs may show small focal necroses with lymphocytic infiltrations. The histological changes observed in humans are usually similar to those occurring in infected animals. Varying pathological changes have been noted in some cases.[21-23]

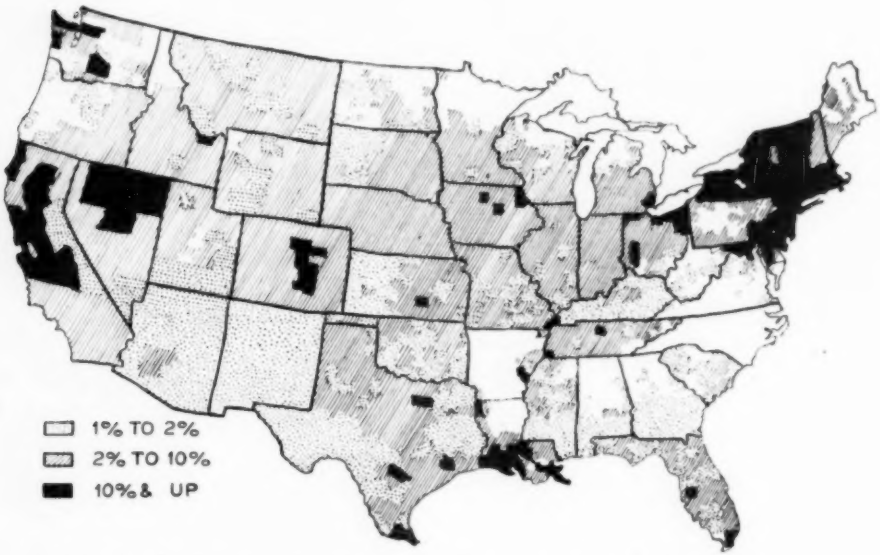
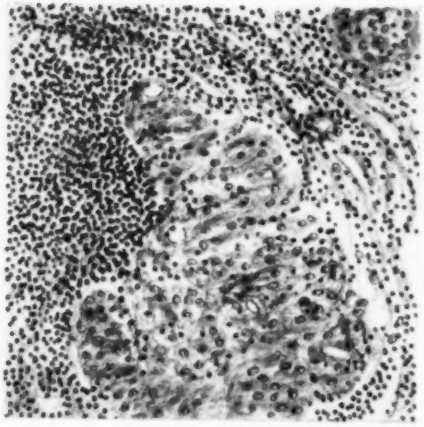


Fig. 2. Distribution of cattle with Brucellosis in the United States in 1943.



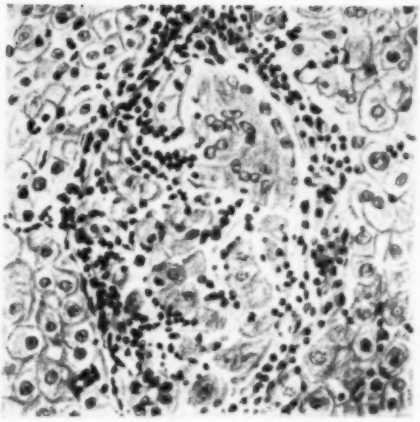


Fig. 3 (left). Human liver showing a nodule comprised of epithelioid cells surrounded by lymphocytes; x 100. Fig. 4 (right). Human spleen showing sarcoid-like lesion; x 175.

Sources and Modes of Infection

Brucellosis occurs chiefly in cattle, hogs and goats but horses, dogs and chickens may occasionally contract the infection. Humans generally contract the infection from these animal sources and rarely from other humans. It has not been possible to show that it is transmitted by human carriers. The infection is acquired as a result of drinking raw milk from diseased cows, by contact with infected animals or by handling infected meat. Cheese and butter made from raw milk from diseased cows also carry the infection since the organism is resistant to the souring process. Tests have revealed that the organism is capable of remaining viable for 10 days in refrigerated milk, and for 4 months in refrigerated butter.[24] The infection may take place through the skin as well as through the alimentary tract. There are records of infections acquired by bacteriologists and others in laboratories both in the United States and other countries.[14, 19]

Examination of humans with brucellosis has revealed that 10 per cent of the patients give off the organism in the urine and some few in the feces. Although there is no evidence supporting the transmission of the disease by human carriers, humans do carry the organism in that the organisms have been cultured from the stool while the individual is in the chronic stage of the disease. Human milk and fetuses have also been found to harbor the organism.

There have been experiments conducted in regard to transmission of this infection by insects such as mosquitoes and biting flies and the results have shown that it is a possibility but no epidemiological data are available to substantiate whether or not this is an important factor.

Occurrence

Brucellosis may occur at any time of the year but it is most frequently found in the summer months when the milk is believed to be more heavily contaminated. Isolation of organisms from abscesses, urine, feces, and blood cultures have shown that the porcine type predominates with the bovine type making up the balance. The caprine or goat strain is found occasionally and can usually be traced to foreign sources. Cattle may also be infected by the porcine type and in turn transmit it to man through the milk. The disease may be brought about by fewer organisms of the porcine type than of the bovine type because they are

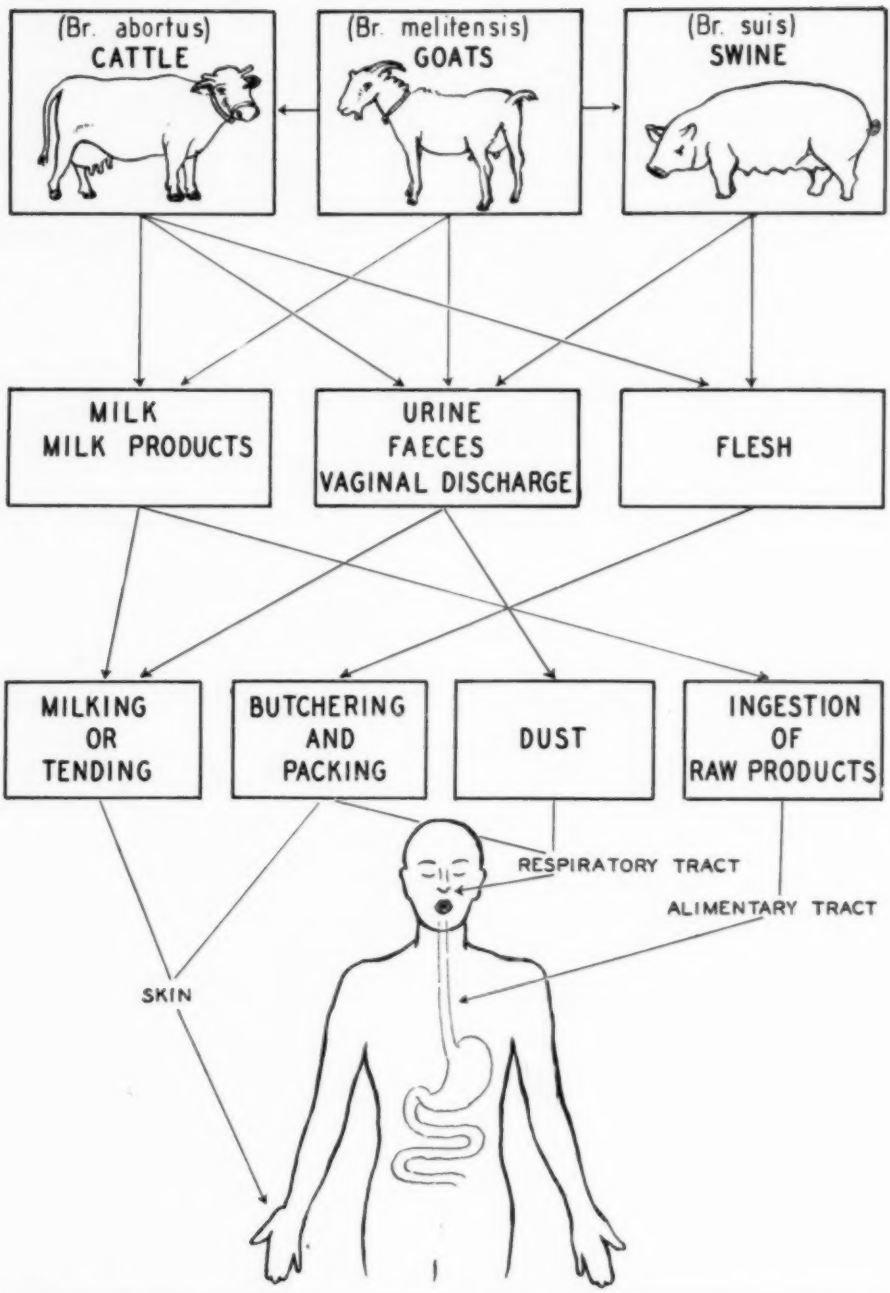


Fig. 5. Epidemiology of Brucellosis.

more invasive in humans. The organism is destroyed by pasteurization so that milk thus processed is not dangerous.

Types of Brucellosis

Brucellosis was first classified in 1897. There are three main types based upon differences in temperature curves. They are: the malignant, the undulant and the intermittent. There are also mentioned an ambulatory form and irregular, mixed and chronic varieties.[25] The classification is not of particular value in diagnosis but it does provide a means of clinical description.

Incubation Period

In a study of brucellosis it was found that there is an incubation period between the time of exposure and onset of actual symptoms. In cases suspected to be caused by *Br. melitensis* the incubation period varied from slightly under a week to 3 months or more with the average being about 2 weeks.[26] Another study revealed a period of 10 days to 2 months.[27]

In infections due to *Br. abortus* the incubation period varied from 5 to 15 weeks with a medium of 10 weeks. The incubation period for this organism is considered to be variable and prolonged.[28] In experimental infections with *Br. suis* the incubation period varied from 11 to 28 days.[29]

SYMPTOMS

A. Undulant Type

The onset of brucellosis may be insidious or sudden but usually is gradual. The symptoms first noted generally are malaise, muscular and cervical pain, anorexia and headache with evening fever. Over a period of about 10 days these symptoms gradually intensify in a manner similar to the course in typhoid fever.

Brucellosis is characterized by a number of symptoms all of which may not appear in every case. Of these symptoms weakness is othe one most common in all cases. In some mild cases it may occur only in the afternoon and may be the only symptom observed. It is usually experienced in the period of onset and in two-thirds of the cases during the fastigium it is most prominent or severe. When convalescence begins weakness is the most persistent. Marked sweating, generally in the morning, or soon after midnight is another common symptom usually of short duration but in some cases may be prolonged. Chills, too, are quite commonly a symptom but are relieved usually by additional covers, clothing, or external heat. This symptom generally disappears when the patient becomes bedfast.

True rigors occur in about one-third of the cases and particularly in the more severe cases. These are suggestive of pneumonia or malaria. They usually do not occur unless the patient experiences the periods of chilliness.

The patient becomes irritable, restless and tremulous. He suffers from insomnia, is in low spirits mentally, and may have a childlike manner, ready to shed tears at any time. In some rare cases there may be an unreadiness of speech, aphonia, or a temporary loss of sensation or motion in the extremities and there have been observed defects of vision, hearing, smell or taste.[14]

In some severe cases anorexia is profound but may be entirely absent in the mild cases. Frequently it varies directly with the degree of fever. Nausea and vomiting occur in a small percentage of moderately severe infections and constipation in one-half to two-thirds of the cases. Constipation is usually marked but may vary with the severity of the disease. Diarrhea is rarely present. Examination of the tongue usually reveals a coated organ with the tip and edges clean.

Many patients have a hacking, non-productive cough accompanied in some instances by a mucoid or mucopurulent sputum. Because of this it is possible for cases of brucellosis to be diagnosed as bronchopneumonia or miliary tuberculosis. Careful attention should be paid to any acute respiratory symptoms and lesions because it is possible that they may lead to further complications such as a pulmonary abscess.[18] There have been reports of culturing *Br. abortus* from tonsils and *Br. melitensis* from the sputum.[30, 31]

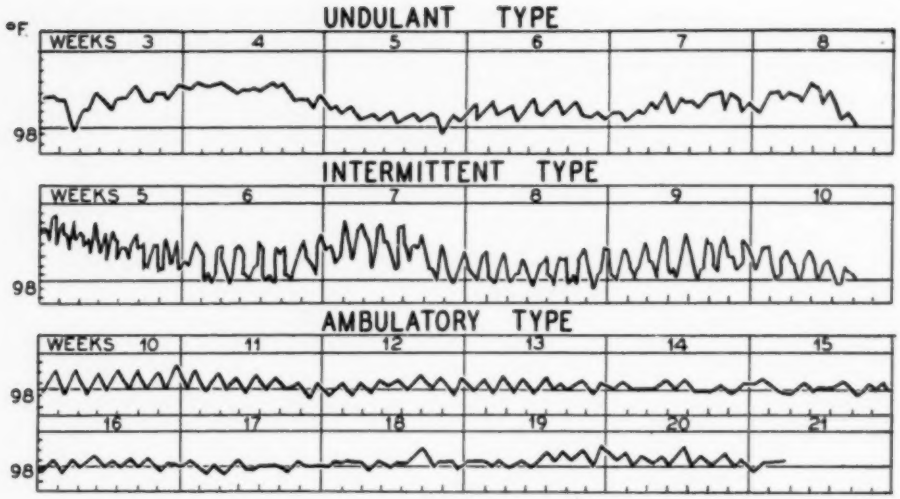


Fig. 6. Temperature curves in different types of Brucellosis.

Some patients may experience a burning pain on micturition and frequent micturition. Excessive sweating may cause a decrease in urinary output.

During the course of the disease palpitation and symptoms of an irritable heart may be observed. In some cases the continuance of these symptoms makes them important as sequelae. Dizziness may be noticed in the beginning or during the most intense period of the disease. The pulse rate usually varies with the fever and bradycardia also may occur. Other symptoms with respect to the cardiovascular system are generally a result of other complications.

As the disease progresses there is a gradual loss of weight and in both severe and prolonged cases emaciation is marked. This is especially true of patients who continue work while suffering from this disease.

In many cases of brucellosis pain is almost completely absent. However, because of the wide distribution of the infection in the body, aches and pains may occur in almost every portion. Patients who continue their activities usually have general aching throughout the body which is aggravated by exercise. Bilateral and frontal (rarely occipital) headache is observed, chiefly in the early stages of the disease and usually in close association with the fever, appearing in the afternoon and increasing in severity in the evening. Occasionally there is also pain in the eyes.[13]

The spleen may be enlarged to percussion and in a few cases is palpable.[14] The lymph nodes are sometimes enlarged.[19] Epistaxis or intestinal hemorrhage occasionally occurs.

In a majority of cases there suddenly appears an intense sacro-iliac pain or sciatic neuritis which lasts for 3 or 4 days. In the early stages there may be a mild pain in the lumbar region, in the back of the neck or there may be a "stiff" neck. The knees, ankles, hips and shoulders may develop pain accompanied by tenderness and swelling for a day or more early in the course of the disease and recurring later.[14] Some patients experience definite and severe abdominal pain either cramplike or continuous in nature. In the mild cases this more or less blends in with the general aching and cannot be localized.

Examination of the blood will reveal a slight leukopenia accompanied by a diminution in the myeloid elements and a relative increase in the mononuclear cells. Some of these latter elements may be pathologic. There is active lymphocytosis and a marked increase in the number of immature lymphocytes in the peripheral blood.[22, 23] The sedimentation rate may be slightly elevated but usually it is normal. Some have reported that the coagulation time is prolonged and clot retraction imperfect.[22] Presence of the organism in the blood is revealed by bacteriological culture. After the first week of the disease agglutinins to one or more stock strains of the organism generally appear in the serum. However, this is not the rule for they may not develop at all.

Brucellosis, commonly known as undulant fever, was given this name because the temperature records have a wave-like appearance. The temperature is increased daily in steplike fashion in the evening until a high of 104° to 105° is reached. After a period of a day or so of high continued fever the temperature declines in the same steplike fashion until it reaches the normal level. As the normal level is attained the constitutional symptoms gradually disappear. The entire cycle lasts for six days to 3 weeks. Another cycle may follow in close succession after a day or two of normal temperature or it may not recur for a considerable period of time. Some patients experience a close succession of cycles for months or more than a year whereas others may have as few as two cycles a year. The average attack lasts for approximately 3 months.

The first wave of the undulant type resembles an attack of influenza and in the second wave the symptoms are intensified and are accompanied by headache, constipation and insomnia. Sweating may occur in the first wave but usually does not develop before the second wave.

This undulant type of fever occurs in approximately 15 per cent of the cases in the United States. It may be caused by the *Br. melitensis* which is predominant on the Island of Malta and in the Pecos Valley of Texas as well as by the *Br. abortus* and *suis* which are found all over the United States. Infection from the former is not usually found in Texas and Arizona.[14]

Infections caused by *Br. melitensis* generally are more severe than those caused by *Br. abortus* and *suis*. In the latter infections the course of the disease may be the same as that of *Br. melitensis* but usually the temperature rises irregularly. Relapses are more common in cases caused by *Br. melitensis*.

B. Malignant Type

The malignant type of brucellosis caused by *Br. abortus* or *suis* is rarely encountered. The onset of this disease is sudden, the course is acute and usually results in death. The temperature rises to a high level where it is sustained. Just prior to death an extreme hyperpyrexia occurs. All of the characteristic symptoms are greatly intensified. As the condition progresses delirium and coma develop. Sweating is not profuse. Splenomegaly is generally observed. Cases of this type usually are terminated in approximately 3 weeks.[18]

C. Intermittent Type

The intermittent type of brucellosis has an insidious onset. The patient has a feeling of afternoon weariness which increases each day. The symptoms of this type of fever are the same as for the undulant type. The severity of the disease varies from a mild to a prolonged infection resulting in death. The temperature generally rises in the evening to between 101° to 104° F. and in the morning declines to between normal and 100° F. In some cases undulatory waves may be superimposed. In the mild cases the temperature gradually subsides until the normal level is attained. Overexertion too early in the convalescent period results in a recurrence.[18]

D. Ambulatory Type

The ambulatory type of brucellosis is relatively short and mild and many patients continue their work throughout its course. The onset is insidious and the patient may

become easily fatigued, feel weak and have a headache. There may be a slight fever. No abnormality may be observed upon physical examination. The spleen may be palpable in some cases. This type of infection may last for 2 weeks to 4 months but usually it runs its course in more than one month but less than four.[14, 18]

E. Atypical Chronic Type

The atypical chronic type of brucellosis is also known as the asymptomatic type. In the infections classified under this heading the diagnosis is extremely difficult because the symptoms are so characteristic of other diseases. For this reason laboratory tests are necessary for accurate diagnosis.

Sequelae

Brucellosis may be of very short duration, the fever lasting only 6 days, but the weakness, fatigability, irritability, stiffness or pain of muscles or joints, backache, headache, general aching, palpitation, sweating and anorexia may continue for some time. Weakness and fatigability are the most common sequelae.

Complications

Rheumatic or arthralgic manifestations develop in the later subacute stage of brucellosis whereas hot swollen joints and/or synovitis are rare complications according to some authorities.[34] Another report confirms this in that arthralgia was found in 32 per cent of the cases studied and inflammation of joints in less than 2 per cent.[35] Others found that arthralgia is commonly found in brucellosis patients but arthritis is rare.[36] Still another source included fibrositis, neuritis, synovitis, arthritis and spondylitis in their listing of rheumatic manifestations. This report stated that the synovitis occurs suddenly, usually while the patient is asleep. The attack lasts for 24 to 48 hours and is entirely gone in a week's time. The joints of the knees, ankles, elbows, wrists and fingers are swollen and very painful but local redness is absent. Examination of fluid withdrawn from the joints reveals that it is sterile but lymphocytosis is present. Arthritis is more frequently encountered than synovitis. It occurs chiefly in the subacute stage and lasts for a longer period of time. The nature of the arthritis is usually monoarticular and resembles tuberculous disease of the hips when found in children. Roentgenographic findings are frequently absent in this condition.[18] However, in spondylitis caused by brucellosis there have been described destructive lesions of the lumbar vertebrae. It is thought that spondylitis is the most common complicating disorder of the bones and joints in undulant fever. It usually occurs in the subacute stage but also may occur any time from 3 weeks to 1 year after the onset of symptoms.[37] Other reports of spondylitis due to brucellosis also have been made.[38] Intermittent hydro-arthritis has also been reported as a complication.[13] A very recent report also has given evidence that *Br. abortus* infection can cause sacro-iliac arthritis. Destruction of the joints begins and results in a local abscess which is healed by ankylosis of the joint.[34]

Many other conditions complicating brucellosis have been reported as follows: brucella meningitis (with recovery);[39] endocarditis simulating subacute bacterial endocarditis; pericarditis; mastitis; mycotic aneurysm of the basilar artery; chronic *Brucella* peritonitis with tuberculous salpingo-oophoritis; cervical lymphadenopathy clinically and histologically undifferentiated from Hodgkin's disease. *Brucella* has been isolated from aspirated bile, from urine in cases simulating cystitis and renal tuberculosis; from pleural fluid; from uterine discharges after abortion and from a cyst on a normal ovary. Uveitis is frequently encountered in areas where the disease is epidemic.

Other complications have included obscure ocular diseases, ulcerated mouth and tonsils, chronic bronchitis, atypical pneumonias, endocarditis, epididymitis, orchitis and ovaritis. It is possible that some human abortions may result. Many show a glandular involvement resembling Hodgkin's disease. In some cases the skin develops purpura or a rash resembling typhoid fever. Eczema or ulcers are also

Fig. 7. **Brucella abortus; x 1,800 seen in a culture growth.**

possible.[40] Suppurative lesions of the gallbladder and appendix have also been observed.[19]

Diagnosis

Diagnosis of brucellosis is made only tentatively from the symptoms described previously and confirmed by blood culture. Cultures may not be positive in some cases, especially the chronic type, but a positive culture is the one certain diagnostic finding.[19] In most cases due to *Br. melitensis* the organisms are present in the blood in the early stages of the disease but in those caused by *Br. abortus* they are less frequently found in the early stages. The blood sample should be taken at the onset of a fever cycle. However, the organisms may be found in the blood after the temperature has returned to normal. In order to prevent the inhibitory effect of the serum a large amount of liver broth and a small amount of the patient's blood is used. If *Br. abortus* is suspected part of the culture should be incubated in an atmosphere containing 10 per cent of carbon dioxide. Because the primary growth is sometimes slow a negative result should not be reported for at least 4 weeks. Usually in a positive culture, growth will be observed in 5 to 10 days. The bovine type (*Br. abortus*) is more difficult to isolate because of its need for CO_2. The other two types grow under both aerobic atmosphere and increased carbon dioxide tension. Splenic puncture usually reveals the organisms more regularly but it is not usually justifiable. Positive results can be obtained in some cases from urine cultures. It may be necessary to make repeated examinations. The urine sample is centrifuged and the sediment spread over the surface of liver infusion agar plates containing 1:700,000 crystal violet. The organisms also have been isolated from stools. The gross particles are removed and to the feces suspension is added an agglutinating anti-abortus serum. Short centrifugation separates the agglutinated bacteria which are then plated out. It is possible also to cultivate the organisms from fluid removed from the meninges, gallbladder and joints.[19]

Guinea pigs, although not very susceptible to *Br. abortus*, can be inoculated with the organism, using blood, tissue, milk or urine.[19] After 4 weeks the animals are killed and cultures made from the spleen, blood and lymph nodes. The laboratory workers should be careful so as not to acquire the infection.

Later in the acute stage of the disease agglutination tests may be employed for diagnosis. The agglutinins may be present in the blood after the fifth day, they may not occur until late in convalescence or not at all. Because proagglutinoid zones may be present in dilutions as high as 1:1200, a number of dilutions should be used. The antigens used are suspensions of the three strains of organisms. Serum dilutions of 1:25 to 1:250 or higher are made up in small tubes. Both antigen and serum are brought to room temperature, mixed and incubated at least 24 hours. Although the temperature of incubation is usually 37° C., it may go as high as 55° C. without harm. A titer of 1:40 is considered as suspicious and 1:100 as positive. If the titer should be below 1:100 another test should be run in 5 to 7 days. If the titer rises the test is significant. A negative reaction does not mean that infection is absent since the ag-

glutinins may not be present. If present, however, they still may be present years after the patient has recovered. It may be necessary to use several stock strains, particularly of *Br. abortus,* because of the antigenic differences in this group of organisms.

Because cross agglutinations occur with *P. tularensis,* serum from suspected cases of brucellosis should be tested for agglutinins with this organism. The homologous species will probably show a higher titer but if the agglutination of both organisms occurs to the same degree, agglutinin absorption tests are necessary for identification.

Another test is the opsonocytophagic test in which is employed the principle that the neutrophilic leukocytes in whole citrated blood of human beings, who have recovered from brucellosis, phagocytize *Brucella* organisms in large numbers in a proper phagocytic system. Leukocytes in whole blood from active cases possess a lower degree of phagocytic activity than do leukocytes from recovered individuals. The leukocytes of individuals with no history of the infection possess very little if any phagocytic activity.[41] Blood is withdrawn from the patient, citrated and mixed with an equal quantity of a standardized suspension of a 48-hour liver infusion agar growth of *Br. abortus.* The mixture is incubated for 30 minutes at 37° C. and then shaken and smears are prepared in the same manner as blood smears. The smears are stained and ex-

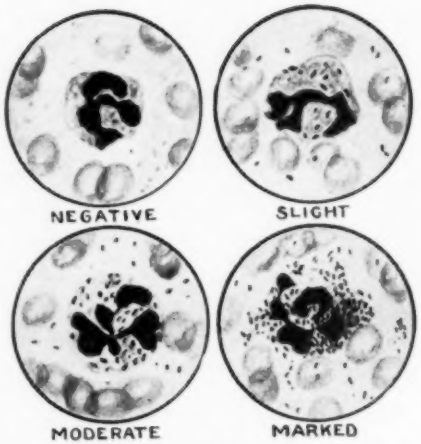


Fig. 9. Phagocytosis of Brucella organisms by polymorphonuclear leukocytes in the Brucella opsonic test.

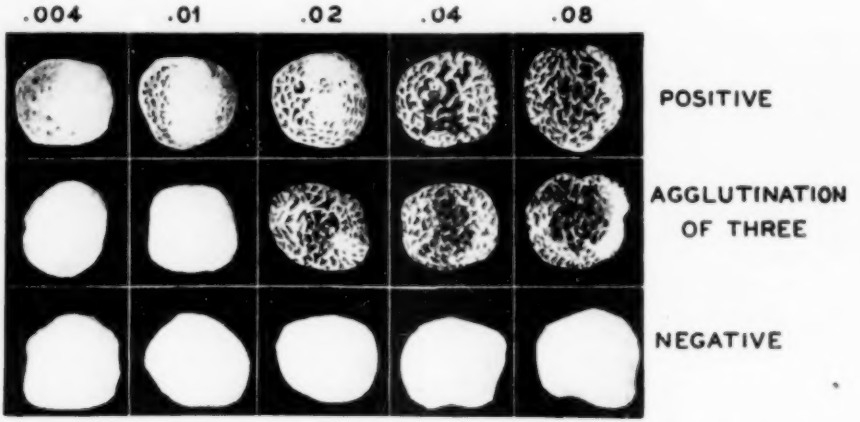


Fig. 8. Rapid agglutination test: Three samples of serum in the amounts of .004 cc., .01 cc., .02 cc., .04 cc. and .08 cc. are shown. A drop of antigen is placed on each amount of serum and slowly mixed with a separate toothpick for each serum. A special glass-plate and dark-field illumination box is used for this test.

amined for neutrophiles. The degree of phagocytic or opsonic activity is determined by counting the number of organisms ingested in 25 neutrophiles. When no phagocytosis occurs the test is negative; slight, when there are 1 to 20 bacteria in the cell; moderate, 21 to 40; and marked when above 40.[13] Another modification of this test uses the following means of classification: leukocytes with no more bacteria than in a corresponding area of the surrounding field are negative; leukocytes with more bacteria than in a corresponding area of the surrounding field are positive; and those considered filled contain 40 or more and are indicated by +. The percentage is obtained by multiplying the number of negative, positive or filled cells by 4. A moderately positive reaction (corresponding to the previous moderate designation) is recorded if 72 per cent are positive with 24 per cent filled; strong if 48 per cent are filled and very strong (markedly positive) if all are filled.[42] A high index has been found in fatal cases so that it does not necessarily imply immunity.[17]

The intradermal test is another aid to diagnosis of brucellosis. This may be done by the vaccine method [43] or the brucellergen method.[41] By the vaccine method 0.1 cc. of a 1-100 dilution of a heat-killed *Brucella abortus* vaccine, containing 2000 million organisms per cc., is injected intracutaneously and the reaction read at the end of 4 days. It is possible that the reaction may be delayed as long as 7 days.[44] The reactions are interpreted as follows: (a) weakly positive—a reddened, indurated area of 5 mm. without surrounding erythema on the 4th to 7th day, but persisting for 10 days or more; (b) strongly positive—areas of redness and induration of 10 mm. or more with erythema and swelling; (c) violent reaction—accompanied by definite systemic reaction such as malaise, fever, generalized aching and an angry axillary adenitis.[45]

In the brucellergen method 0.1 cc. of a standardized dilution of protein nucleate is injected as above. The reaction is read in 24 and 48 hours after the injection. This test is read and interpreted as follows:

E = erythema, no significance.
2 + = edema and erythema two centimeters in diameter, positive.
3 + = edema and erythema more than two centimeters in diameter, positive.
4 + = edema and erythema more than two centimeters in diameter and mild systemic reaction, positive.
5 + = edema and erythema more than two centimeters in diameter and marked systemic reaction, positive.

There has been made available recently a brucellergen product, a protein nucleate, for which the claim is made that it gives no false positive reactions and does not produce the severe local reactions which occur with other such agents.

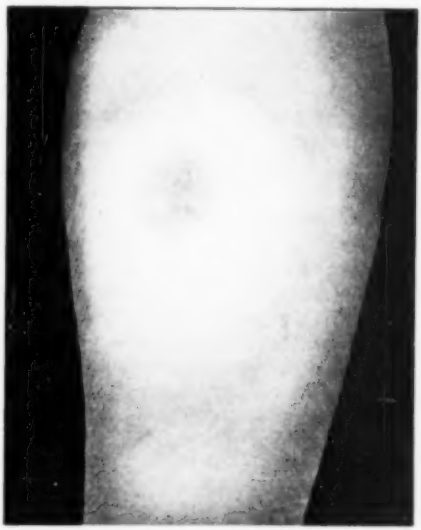


Fig. 10. Positive reaction to the brucellergen test after 48 hours.

Other tests have been suggested, such as the complement fixation test,[13, 46] but this is not used because of the time and work involved and the test furnishes no more

information than can be had in the agglutination test.[45] Some workers have suggested this test as the solution to diagnosis in chronic brucellosis.[47] Another test called the therapeutic test involves the administration of M B P vaccine (a solution of ground organisms of all 3 strains of Brucella)[33] at intervals of 5 days, increasing each subsequent vaccine dose. Reactions which occur include severe malaise, fever and a flaring-up of intestinal manifestations.

Studies of the blood have shown that there apparently is no pathognomonic picture in this disease. Moderate leukopenia with significant neutrophilic reduction, moderate leukocytosis and pathologic lymphocytes resembling those in infectious mononucleosis have been observed.[33, 48]

The red cell sedimentation rate is usually accelerated moderately or markedly but may also remain normal. If there is a negative sedimentation rate accompanying a febrile infection brucellosis can be suspected because it is one of the few infections in which a normal sedimentation rate is observed.[49]

There is a great deal of controversy over the accuracy and value of these laboratory tests. Various comparative studies have been made of the different methods and their modifications. Some have reported good results and others have not been good. It is generally the consensus that none of the tests used individually without the other tests and without supportive history and examination is of value. Several critical reviews of the tests have resulted in the conclusion that isolation of the organism is the only certain method for diagnosis of acute or chronic brucellosis. If positive cultures are not obtained clinical criteria or serologic findings cannot be used alone as the basis for diagnosis. Positive serologic tests are to be considered on the same basis as a positive tuberculin test in the adult. They indicate that the tissues of the patient have had sufficient contact with Brucella organisms prior to the test to react to the testing material. They do not differentiate between past and present infections nor subclinical and clinical infections. The agglutination tests are more reliable than serologic tests during the acute febrile phase. However, they may be negative in about 10 per cent of the cases. In chronic brucellosis they may be negative to the extent of 50 per cent, thus making them less dependable. The skin tests are somewhat more reliable in the chronic stages of the disease but usually show negative results in approximately 10 per cent of the cases. The opsonocytophagic tests usually show false negative results in 3 per cent of the cases in the acute or chronic stages.[45, 49, 50]

It appears to be the consensus that there is no reliable method for the detection of chronic brucellosis despite those workers who strongly advocate the agglutination and dermal tests. If clinical findings alone are used, or even where laboratory methods are used in addition, there is still the possibility of mistaken identity. The laboratory methods with the exception of the positive *Brucella* culture are not always discriminatory.[45]

Another authority has stated that the agglutination tests may be relied upon for diagnosis later in the acute disease and that the opsonocytophagic test is of significance only when used with the other tests. This same worker prefers the brucellergen antigen when the intradermal test is used but feels that a diagnosis should not be based upon this test alone since a negative reaction does not rule out brucellosis and a positive reaction may only indicate that the patient has at some time had a *Brucella* infection.[19]

Another evaluation of the tests has led to the following interpretations: (a) if negative results are obtained in the culture, the intracutaneous and agglutination tests, it is uncertain as to whether the patient has ever had brucellosis and therefore the opsonocytophagic tests have no real significance other than the fact that specific opsonins are not likely to be present unless there has been a past or recent infection; (b) a positive intracutaneous test indicates an old or recent infection of undetermined activity and a violently reacting test is unusual unless the infection is fairly recent or there is evidence of skin contact with *Brucella* organisms; (c) if clinical symptoms of brucellosis are present, the in-

tracutaneous test is positive and the opsonocytophagic test is low, it can be presumed that the patient is not fully recovered from an old infection; (d) if these same factors hold and the opsonocytophagic test is high, the patient most likely has recovered from the infection. The tests are best used as a battery rather than individually.[51]

Differential Diagnosis

Because brucellosis has no pathognomonic signs which definitely differentiate it from other diseases it is frequently improperly diagnosed. It is most commonly confused with typhoid fever, influenza and tuberculosis. Other conditions less commonly confused include malaria; pyogenic septicemia; various respiratory infections such as bronchitis, sinusitis and pneumonia; appendicitis; cholecystitis; diseases of the cardiovascular system such as subacute bacterial endocarditis, pericarditis and hypotension; infections of the urogenital system such as cystitis, pyelitis, pyonephrosis, orchitis and epididymitis; liver abscess; infantile paralysis; spastic colitis; chronic carbon monoxide poisoning; tetanus; neurasthenia; "nervous breakdown"; "eye trouble"; "liver trouble"; acute rheumatic fever and tularemia.[18]

It is important that brucellosis be considered in diagnosing these conditions for if all the facts of the history of the case are known many of these conditions may be eliminated rapidly. Some, however, still provide certain obstacles which can be overcome by careful consideration of the clinical symptoms.

In typhoid and paratyphoid fever the onset of the disease is more rapid; the patient appears dull and toxic; there are diarrhea, tympanites and a sustained temperature. The fastigium is usually very brief in brucellosis and the abdominal signs and symptoms are milder. Although prostration occurs in both conditions, typhoid fever does not cause the pronounced sweating observed particularly in the second wave of brucellosis. A positive Widal test and the isolation of *E. typhi* or *S. paratyphi* is sufficient to establish the diagnosis.[14, 18] It is necessary to isolate the organism in addition to the Widal test because a false positive Widal may be obtained from other conditions.

It has been reported that some 20 per cent of cases are diagnosed as influenza. Because this name is given to all indefinite fevers this is very possible although the real influenza does not resemble brucellosis too closely. Both conditions produce a leukopenia (as does typhoid also), prostration, general aching and sweating. However, influenza is more abrupt in its onset and does not last as long. It is, furthermore, usually accompanied by an upper respiratory infection,[14, 18]

Brucellosis and pulmonary tuberculosis are frequently confused because both diseases have an insidious onset, some weakness, night sweats, loss of weight, anorexia, cough and a low white count. However, tuberculosis usually does not cause chilliness or rigors, constipation, nervous irritability, arthralgia and general aching. Here again, laboratory tests are necessary to establish the diagnosis,[14, 18] In addition to the laboratory tests the presence of a cough, clinical findings and sputum examination also are important.

Malaria may be confused with brucellosis because of the rigors repeated at regular intervals. Laboratory tests, careful history of the case and close observation of the clinical signs are of value in diagnosis.[18]

Although bacteriological cultures and agglutination tests may be necessary to differentiate between pyogenic septicemia and brucellosis, diagnosis may be established by the fact that the latter condition is usually accompanied by a leukopenia or normal white cell count along with a relative lymphocytosis.[18] In pyogenic septicemia there usually also is observed a focus of infection.

The remittent fever, weakness, loss of weight, anemia, sweating, hematuria, joint pains, splenomegaly and, in some cases, petechiae observed in brucellosis of long duration are symptoms common to subacute bacterial endocarditis. In fact there may be an endocarditis brought on by *Brucella* so that differential diagnosis is based upon blood cultures, skin tests, blood

counts and agglutination tests[12, 14, 18] as well as a history of subacute bacterial endocarditis usually suspected in those with previous rheumatic valvular heart disease.

Certain types of tularemia are easily differentiated from brucellosis but in the rare typhoid type there may be some difficulty in diagnosis. This is particularly true if the typical clinical signs are absent because cross agglutination is possible if the agglutination test is used. The serum of tularemia patients is capable of agglutinating *Brucella* antigens in diagnostic titers. Thus it is necessary to conduct agglutination tests for both conditions if there is any suspicion of exposure to *B. tularense*. In tularemia the agglutination titer with *tularense* antigen is higher than that with *Brucella*. The intradermal test described previously also will give negative results in tularemia.[14, 18] Diagnosis is also ascertained by a therapeutic test in that tularemia is said to be specifically responsive to streptomycin whereas brucellosis is not.

Acute appendicitis or cholecystitis is sometimes diagnosed in cases where the disease is actually brucellosis. The presence of fever, abdominal pain and localized tenderness without any consideration for generalized infection may easily lead to this decision. There have been reported cases where appendectomies and cholecystectomies have been performed in cases of brucellosis.[52] After removal of the organs pathological examination revealed no inflammatory processes. It is necessary therefore to study carefully the history along with a thorough physical examination and blood counts. In gallbladder conditions x-ray is of value in diagnosis.

Brucellosis is often accompanied by frequent and painful micturition and pyuria usually occurring late in the invasive stage or during the fastigium, which may lead to diagnosis of a localized genito-urinary disease. In such cases, as well as in orchitis and vesiculitis, a careful study of the history, clinical course and laboratory findings, will lead to the proper diagnosis.[14, 18]

Many cases of brucellosis of long duration in which nervousness, weakness and depression have been the chief symptoms have been diagnosed erroneously as neurasthenia or neurosis. The consequences to the patient of such a diagnosis are serious and may result in a serious mental state and lowering of the morale.[3]

Prognosis

Fatalities of 2 to 3 per cent of the cases have been reported in brucellosis. These have occurred in the ambulant type as well as the malignant type. Infections caused by *Br. abortus* are generally less severe than those caused by *Br. suis* so that the prognosis in the former is more favorable. The duration of the disease varies greatly. Approximately 20 per cent of patients are able to resume normal activity in 1 month; 25 per cent in 1 to 2 months; 35 per cent, 3 to 4 months; 12 per cent, 5 to 6 months; and 8 per cent in 6 months to 2 or 3 years.[14] Although the average is 3 to 4 months cases lasting many, many years have been reported. Because of the great variability of duration the prognosis to the patient should be rather conservative in the estimate of time of duration.

Immunity

It is believed that an immunity to brucellosis may be acquired as a result of subclinical or unrecognized infections. This is based on the fact that agglutination titers of 1:50 to 1:500 have been found in the serum of veterinarians of whom a majority had no history of symptoms resembling those of brucellosis. This has also been observed in butchers and others with no history of the infection.[14, 19]

Prevention

It is rather commonly thought that the control of brucellosis in cattle and prevention of its subsequent transmittal to humans is carried out by destruction of the infected animals. This, unfortunately, is not always true and furthermore is not feasible from a practical and an economic standpoint.[34] It is estimated that 10 per cent of milk cows are infected.[40] Generally the calves and adult cows are vaccinated with strain 19.[53, 54] For control of the disease the

adult pregnant cow should be vaccinated before the fourth month of pregnancy. Necessary sanitary procedures are routine. Infected animals showing a titer of 1:100 or higher should be removed immediately for it is relatively easy for one cow to infect a herd in a short length of time.[34] This and other control procedures established throughout the United States reduces somewhat the danger from raw milk. However, the only practical method for protection of the public is the pasteurization of milk and dairy products. It is estimated that the destruction of cattle which is carried on results in a loss of hundreds of millions of pounds of milk, millions of pounds of butter and 8 million pounds of beef annually.[40]

This does not control the other source of infection, that of infected hogs. Veterinarians and abattoir employees are exposed to the infection particularly. Veterinarians are advised to wear long rubber gloves when tending animals in abortion cases. It is recommended that abattoir employees be given vaccinations with several of the antigens of the *Br. suis* group. Laboratory workers who are going to handle *Brucella* cultures should also be given vaccinations with several antigens.[14]

THERAPY

General Measures

Rest in bed during the course of the acute stage and for 10 days to 2 weeks after the temperature has returned to normal, forcing of fluids, alcohol sponges and ice-caps are indicated as symptomatic treatment just as in the case of any acute infection. Bed rest as described will frequently result in a more rapid disappearance of the fever and other symptoms and aid in shortening the course of the disease.[55] To relieve the irritability and nervousness, phenobarbital or other mild sedatives may be necessary. To relieve the aches and pains, acetylsalicylic acid (but not aminopyrine) may be given. The mental depression which is such a prominent symptom should be given special attention.[14] A diet high in calories and in vitamins is also indicated as a general measure. Until recently, specific treatment of brucellosis still seemed to be far from the goal.

Vaccines

Some years ago a vaccine was developed from the heat-killed *Br. abortus*. Some have expressed the opinion that this vaccine is of value in treating chronic or recurring types of cases, particularly when the agglutinin titer of the patient's serum is low. It is given in a beginning dose of 0.1 cc. of a 1:100 dilution and the dose increased carefully and in accord with the severity of the systemic reaction which occurs. It is administered intracutaneously at 5-day intervals.[14, 44]

Others have expressed the opinion that the value attained with the vaccine therapy is due to the general foreign protein reaction and therefore might also be obtained by administration of typhoid vaccine. The Council on Pharmacy and Chemistry of the A.M.A. no longer accepts *Brucella* vaccine.[56] Still other workers have used the vaccine only after sulfonamides and hyperthermia had failed. The sensitivity of the patient to the vaccine is determined by intradermal test and then the vaccine given intramuscularly every 5 days in increasing doses for 5 or 6 times to induce a moderate systemic reaction. In some cases it is necessary to give the vaccine for longer times.[24] Other vaccines used by other investigators did not give striking results. One group reported that nicotinic acid given intravenously in addition to a vaccine was helpful.[32]

Several vaccines are available commercially from various manufacturers. Some are monovalent in that they contain only one organism whereas others are bivalent or contain two organisms. There are available monovalent vaccines for *Br. abortus* and *Br. melitensis* and bivalent vaccines containing combinations of *Br. abortus* and *melitensis* or *Br. abortus* and *suis*. The strengths range from 750 to 3000 million killed organism per cc.

Antiserum

Some years ago a goat antiserum was developed and employed in a number of cases. After a sensitivity test it is given

intravenously or subcutaneously in doses of 20 cc. daily for 5 days or until improvement is observed. The total average quantity given is 90 to 120 cc.[57] Horse antiserum is also given in the same manner. Another investigator used bovine serum with some value.[58] After the eighth month of the disease serum therapy is not advisable. It is necessary also to consider the possibility of serum sickness which would add to the discomfort of the patient.[14]

There is available commercially a polyvalent antibacterial serum in dry form made from the blood of cattle immunized with all three of the organisms. It is administered intravenously or intramuscularly to adults in doses of 50 cc. of the restored serum in severe cases until a total dosage of 100 cc. to 150 cc. has been given in 48 to 72 hours. For children under 13 years of age it is given in divided doses according to the weight. In these cases it is administered intramuscularly or subcutaneously.

Hyperthermia

Hyperthermia also has been employed to treat brucellosis with varying but somewhat favorable results. In this type of therapy fever is induced in the Kettering hypertherm. Favorable results have been attained in acute and subacute cases,[59] in chronic cases and in brucellosis spondylitis.[37] Indifferent results were obtained by other investigators.[60]

Blood Products

Frequent small transfusions of 250 cc. of blood by the indirect method and obtained preferably from donors immunized against *Brucella* are recommended in those cases which are prolonged.[14] Some workers have reported rapid improvement in a patient when given 250 cc. of citrated blood intravenously from an immunized donor.[61] Others have been given 500 cc. of citrated whole blood from a recovered patient with good results.[44] Human immune serum has been given intraspinally in doses of 15 cc. 3 times a day on alternate days and once a day on successive days in cases of meningitis.[62] Ordinary convalescent serum has also been investigated. Some have also used whole blood giving 1 or 2 transfusions by the usual method with favorable results.[63]

Brucellin

Brucellin, made from the filtrate of a broth culture of 3 strains of *Brucella*, and containing the nucleoproteins of the organism in a mildly alkaline solution, has been used with some success. A preliminary intradermal injection of 0.1 cc. of the brucellin is given and if in 24 hours there is no marked systemic reaction 0.2 cc. intradermally and 0.8 cc. intramuscularly are given in the afternoon or evening. The systemic reaction induced is repeated 3 or 4 times every 3 days. Treatment of a number of cases with brucellin has shown favorable results according to some workers.[13] Another method of administration is to give 0.1 cc. intracutaneously every 5 days increasing the amount by 0.1 or 0.2 cc. until 1.0 cc. is given. This is followed by a similar regimen with a 1:10 dilution. Some patients may experience marked systemic reactions to 1.0 cc. whereas others have no discomfort. It is necessary by means of graduated dosages to desensitize patients having high agglutinin and cytophagic indices and a markedly positive skin test with brucellin.[14] No specific results were reported in the use of brucellin given every 3 to 5 days until 3 doses had been given, which seems to add a disadvantage.[55] Other investigators state that brucellin is not the agent of first choice to be used in the acutely ill patient.[24]

Recently there was made available commercially a brucellin antigen which consists of a clear, cell-free culture filtrate prepared from selected, virulent strains of *Br. abortus*, *Br. melitensis* and *Br. suis*. It is claimed that 85 per cent of patients, with brucellosis and in whom the infection is active, respond to therapy with this product.

Sulfonamides

As is usual in the discovery of any new therapeutic agent its value is tested in many conditions for which there is no specific

therapy. The sulfonamides have been tried and at first were thought to have some value but recent investigations have shown that they do not cure the acute or chronic forms of brucellosis.[44, 63]

Penicillin

In vitro tests with penicillin against *Brucella* showed promise but in clinical trials no value was shown.[56]

Streptomycin

Streptomycin, too, has been tested for its value in the treatment of brucellosis. In some patients there was a decrease in fever whereas others were not affected. In those in which the fever was decreased no relapses had occurred in 8 weeks. The dosage given to those cases showing improvement was 4 Gm. daily for 14 to 21 days whereas the others received only 2 Gm. daily.[64] There are also on record cases where the blood level of streptomycin greatly exceeded that necessary to kill the organisms *in vitro* but the infection continued. In the overall summary on the status of streptomycin the dosage recommended is 4.0 to 5.0 Gm. intramuscularly or subcutaneously every 3 or 4 hours for 10 to 14 days but it is also stated that clinical results are disappointing.[65]

In treating sacro-iliac arthritis due to *Brucella* with streptomycin no conclusive evidence could be given because it was admitted that it had not been used for a sufficiently long period of time.[34]

Recent reports of the use of streptomycin and sulfadiazine in the therapy of brucellosis have shown more promise than any other therapy.

In recent experiments with chick embryos infected with *Br. abortus, Br. suis* and *Br. melitensis* organisms it was found that streptomycin alone in a dosage of 40 micrograms first prolonged the survival time which became maximum with the dose of 320 micrograms. Protection with sulfadiazine alone was first observed with a dosage of 0.12 mg. and the maximum was reached with a dose of 0.48 mg. In combination protection was first observed with 20 micrograms of streptomycin and 0.03 mg. of sodium sulfadiazine and reached a maximum with a dosage of 40 micrograms of the former drug and 0.06 mg. of the latter drug. It was stated that the combined therapy results in a synergistic effect which eliminates the *Brucella* organisms from the chick embryo tissues.[66] Successful treatment of 2 patients with acute brucellosis was first reported in 1947 and later similar results were attained in 3 of 4 additional cases. The dosage employed was 0.5 Gm. of streptomycin intramuscularly and 1 Gm. of sulfadiazine orally every 4 hours for 14 days or more. At this time it was still too early to state that permanent arrest of the disease was obtained but further trial was recommended. In most cases there was a prompt remission which was sustained. In the one case which did not respond *Brucella* could not be cultured from the patient.[67]

Because of this evidence of the suppressive action on *Brucella* of the combined therapy, other workers investigated its use in a case which appeared to have the ideal characteristics necessary for the evaluation of therapeutic agents. Large doses of streptomycin and sulfadiazine used separately produced no effect on the clinical course, the fever or the septicemia. After the separate course of streptomycin was given a 28 day course of sulfadiazine was begun. The daily dose of 4 Gm. was progressively increased to 12 Gm. so as to maintain blood levels at approximately 10 mg. per 100 cc. No improvement was noted in 18 days. At this time streptomycin in doses of 6 Gm. daily (total used was 62 Gm.) was added to the therapy. During this period the blood cultures became negative, the fever dropped sharply in the first half of the period, then climbed sharply and dropped again right after therapy was discontinued. A prompt clinical and bacteriological cure was effected.[68]

Another report found that 9 patients treated with a combination of sulfadiazine and streptomycin yielded more satisfactory results than any other therapy in human brucellosis. The recommended dosage of streptomycin is 0.5 Gm. intramuscularly every 6 hours for 7 days and of sulfa-

diazine, 4 Gm. orally and then 1 Gm. every 4 hours for at least 2 and preferably 3 weeks.[69]

A later report states that this combined therapy has been found of value in treating a case of chronic brucellosis of the *Br. suis* variety. Streptomycin in dosages of 4 Gm. and sufadiazine in dosages of 6 Gm. daily were given approximately 1 year after onset of symptoms. After 5 days the dosage of streptomycin was reduced to 2 Gm. daily for 3 days and then to 1 Gm. for 19 days (total 44 Gm.). The dosage of streptomycin was reduced because of the improvement shown in 48 hours at the end of which time the patient had no fever or symptoms. No toxic effects from streptomycin were noted. When reported the patient had had no relapse in 4 months.[70]

Polymyxin

Other antibiotic drugs also have shown value in the therapy of brucellosis. Polymyxin, still under investigation, is derived from *B. polymyxa*, an organism found in soil, water, sewage and mud. Polymyxin has been used to treat human cases of brucellosis caused by *Br. abortus* and has been found to have a therapeutic effect. Total daily dosages as high as 5 mg. per Kg. of body weight were given in a specially prepared buffer solution of pH 7.4. The dose was divided into 8 equal doses and given at 3 hour intervals. In those cases where a total daily dose of 3 mg./Kg. was given an examination of the serum revealed concentrations of 0.6 to 1.3 mg. per cc. 24 hours after therapy. Urinalysis revealed detectable amounts in 12 hours after the therapy had been started; in 24 hours the urine showed effective bactericidal concentrations.

When compared with streptomycin, polymyxin was found to be 5 to 10 times more effective in the control of experimental Gram-negative infections. Dramatic response has been noted with this drug in treating acute brucellosis. The toxicity of the present specimens of polymyxin preclude any general use of this antibiotic.

Aureomycin

Aureomycin is an antibiotic extracted from one of a new species of the Actinomycetes, *Streptomyces aureofaciens*. Recent reports have shown promise for this drug in the therapy of brucellosis also. When tested against five strains of organisms belonging to the *Brucella* group it was found to be an effective bacteriostatic agent in concentrations of 0.75 micrograms per ml. or less. Aureomycin possess a low toxicity when given orally and it is effective therapeutically in oral dosage. It may be given in relatively large amounts such as 1 Gm., 4 times daily for several days.

A recent report of the clinical trial of aureomycin in the therapy of 24 patients with acute and chronic brucellosis due to *Br. melitensis* has been published. The drug was given orally and the immediate therapeutic results obtained surpassed those obtained with any other therapy including the combined streptomycin and sulfadiazine routine. The dosages recommended are a total of 1 Gm. given the first day in four divided doses, a total of 0.6 Gm. the second day, 1.6 Gm. the third day and 2 Gm. the fourth day. The drug should be administered for a total of ten days. Until more is known about the Herxheimer-like reactions which occur with larger initial doses and the quantities necessary for permanent recovery the above dosage is advocated. The febrile reaction is usually associated with a drop in blood pressure unless the initial doses are small. Further bacteriologic studies following therapy have shown that larger doses of aureomycin prevent bacteriologic relapses so that the total daily dose recommended is 4 to 6 Gm. for a week instead of 2 Gm.[71]

Surgery

Some have expressed the belief that the *Brucella* organisms imbed themselves in certain foci which drugs cannot reach and therefore they feel that surgery is indicated. Gall bladders have been removed and some splenectomies have been done as a result but the results have not been striking.[56] In those cases of long duration the gallbladder and prostate should be examined as possible localized foci. If this has occurred and a sulfonamide combined with diathermy treatment daily (through the

site of localization) does not relieve it, surgical excision may be necessary.[14] It is hoped that the combined therapy with streptomycin and sulfadiazine or therapy with aureomycin will eliminate this necessity.

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The Problem of the Sexual Offender

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Public indignation when judges mete out light sentences to sexual offenders is entirely understandable, but it is based on emotional reaction and does not reflect a realistic approach to the problem.

The public for the most part believes that people who commit "sex crimes" belong to a very definite category—that they have had a poor education; are poor economically; come from poor surroundings; have been in difficulty in the community before and possibly have been arrested for other crimes; and that they are individuals who do not get along with their families and children.

From a psychiatric standpoint, we find these conditions to be far from true. In other words, a great many people who commit sex crimes pass in the community as entirely normal individuals. In fact, many of them are regarded as model citizens, are apparently well-adjusted in their homes, excellent workers, good family providers, and often churchgoers.

Because we find such a multiplicity of circumstances, it is quite obvious we must look much deeper than the surface for clues as to the reasons for their behavior. In the majority of cases, and particularly so in those who repeat the crime, we find individuals who did not develop emotionally; that a great many of them have never achieved what is termed a true heterosexual level, or emotional maturity. In other words, they have not passed through the stages which emotionally mature persons go through and leave behind them.

Many are still in the narcissistic stage in which the individual lives only for himself. This is the earliest emotional stage a person goes through. When such an individual finds the world does not exist for him alone, but has hardships which must be faced, conflicts are often set up within him. He may be unable to face these conflicts and they are buried in his personality. Later on in life they may be reproduced under circumstances similar to those which created them, producing considerable emotional tension.

Many sex criminals remain in the next, or homosexual, stage, which is an entirely normal one in the process of emotional development of the child. In this stage, the individual shows a marked inclination for his own sex. Small boys who gather in gangs and label other boys who won't indulge in rough play "sissies" demonstrate this stage. Little girls grouping together and looking down on little boys also demonstrate this particular process of emotional development, but seek each others' comfort and protection for self enjoyment.

Many persons who commit sex crimes have never gone beyond these stages to the third, the heterosexual stage, or if they do reach it find it too difficult to maintain and slip back when confronted with life's problems. This stage, in which the individual is preoccupied with the world about him as well as with himself, and in which he shares an interest in the opposite sex, leads to maturity. Most persons reach it between the ages of 14 to 20 years.

Individuals who remain in the first stage are usually the exhibitionists and those who demonstrate various types of sexual perversions.

Individuals in the second stage are the ones who indulge in assaults on children or members of the same or opposite sex. We find in the latter case that most of these sex criminals come from homes in which there were either over-solicitous or domineering parents of one or the other sex.

It is impossible for anyone to look at a group of persons and tell who is likely to commit a sexual assault.

A very significant study made recently

in a Chicago municipal court of 100 sex offenders demonstrated how incorrect are the usual notions of the public about sex offenders. How difficult it is for society to handle these cases of "sexual irregularity" may be seen by looking at the findings of this study.

Of the 100 men studied, 84 per cent committed sex crimes before they were 40 years of age. Over 40 per cent were married.

Whereas the public believes Negroes commonly are implicated in sexual assaults, the study revealed that the proportion of sexual crimes involving Negroes was much lower than that involving white people.

The common belief that most sex crimes are committed in public places was shown to have no basis in fact when it was revealed that only 33 irregularities were committed in such places as streets, parks, beaches, theaters and other public places. Fifteen per cent were committed right in the victim's home, 52 per cent very close to home.

Nearly 75 per cent of the assailants committed sexual irregularities in broad daylight, the rest in early morning or if at night under artificial lights—an indication that there is no basis for the popular misconception that sexual criminals always spring from behind trees on dark, lonely streets.

The cases analyzed revealed almost as many assailants to be of the Protestant as Catholic faith with a proportionate sprinkling of Jews and Christian Scientists. Almost 50 per cent were regular churchgoers, 25 per cent attended occasionally, and 25 per cent not at all. This refutes the argument of those who believe the answer to the sex problem lies only in making people attend church regularly as a deterrent. It may help, but the problem begins much earlier and is much deeper.

The educational background of these offenders was no different than that of a proprotionate number of men who had not committed sex crimes—in fact, there was a slightly higher number of college men in this group than in the average group of men.

The sexual history of this group likewise reveals that sexual offenders do not belong to any one group. A very small number had committed sex crimes before, and only 5 admitted to perversions. Only 21 of them were revealed not to have had normal sexual relations previously. The popular conception that sexual offenders are usually perverts was therefore shown to have little basis in actuality.

The study demonstrated that 35 per cent of these individuals were definitely unstable emotionally, that 41 per cent came from broken homes (this includes the 35 per cent of unstable persons)—but leaves the greater percentage in the apparently stable group.

An even more significant study is one which was made in the Army among 270 sex offenders. Remember that all these persons had been screened by psychiatrists before entering the service. Yet the study revealed that it is almost impossible to detect the sexual offenders as a definite type of person showing well defined symptoms of sexual abnormality.

Age had no significance in this study since it was a young group. As in the previous study, the Negro was found to have committed fewer sexual offenses in proportion than the white person. Almost 65 per cent of the total group came from the city; more of the offenders came from the skilled (professional) than the unskilled or semi-skilled class. Their mental age (intelligence) was in the normal range, and before the commission of the irregularity 60 per cent were considered of good personality—neither extreme introverts nor extroverts. Thirty per cent were introverted personalities, 10 per cent extroverts.

Sixty per cent of the cases revealed no history of definite mental or nervous disorders in the family. About 7 per cent had a history of a mental illness in the family and 7 per cent came from families of chronic alcoholics.

Almost 80 per cent were unmarried. (This group was a young group with the majority 18-22.) Of the 20 per cent married, significantly 40 per cent were either divorced, separated, or widowed.

The great majority were regarded as law-abiding citizens, with only 2 per cent with a history of ever having been arrested for more than minor offenses. Seventy-five per cent of them had never been arrested, or fined for any cause.

Only 2 per cent were chronic alcoholics, and 46 per cent were moderate drinkers. Thirty-five per cent said they were excessive alcoholics, but much of this drinking was done in the armed services and does not indicate drinking habits prior to entry into the services.

About 3 per cent had used narcotics; the incidence of illness and accidents in their past life was very low, as was the incidence of venereal disease. The occupational history of the group indicated that most of them were steady workers in civilian and army life.

The group had a very high educational level, higher than average. However, 40 per cent came from unstable parents. This is of great importance. In temperament, the offenders often showed keen musical and dramatic ability.

In summary, the individuals who commit sexual offenses are extremely varied and come from all grades of society. Although the public becomes upset over sexual irregularity, the fact remains that the vast majority of offenders never repeat such acts. Studies show their behavior, for the most part, to be impulsive and in the majority of cases getting caught is sufficiently shocking to them to effect avoidance of the offense in the future on their part.

Most of them come from a good economic level, have god jobs, and families who depend upon them. They are capable individuals, frequently with intellectual gifts of a high order.

The important consideration in the handling of such cases by the court is the determination of factors involved. The judge must try to assess the nature of the offense, previous adjustment in the community, to the family, in work, and among acquaintances, and determine whether or not this is an impulsive, isolated act, or due to personality (emotional) defects; or one of a series of acts. The latter are the most serious and require treatment, often institutional care.

Social service studies, as well as psychiatric studies, of not only the individual, but of his home and other members in it, are valuable. A judge who metes out a sentence without such studies often aggravates an unstable personality so that when the culprit is free he is in greater difficulty and is far less able to maintain a degree of stability. It is important to remember that the people who are so-called "normal," as far as the community is concerned, may not be so, and that many of such offenders under treatment and guidance will in all probability never repeat such a criminal act. It is important to weed out the individual who is a chronic offender from the former. A combination of psychiatric and social aid, as well as calm, unhurried judgment, is requisite in a judge trying such a case.

This is the reason why modern judges who are well versed in this field mete out variable sentences for apparently similar acts. They have assessed such individual offenders, not for the offense, but on the basis of personality defects. The man with or without a record should have some psychiatric investigation and treatment in the court, hospital, or penitentiary. There is no question that recidivists and those who will be repeaters for the rest of their lives must be segregated, but they are a small proportion of the total number and for them such institutionalization should be provided which will give them an opportunity to relieve their emotional problems and provide outlets so that they can be useful persons and employ whatever intellectual skills they have, and at the same time place them where they can cause no harm in the community.

The solution for the future lies not so much in the treatment of the individual as it does in the early provision of sound mental hygiene habits in the home and community. The point of attack is the parents. It lies in taking the present young generation and teaching it good, healthful mental hygiene practices so that it can adapt its own life to the conflicts of the world which surrounds it and learn how to endure pain, frustration and disappoint-

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Methods of Improving the Peripheral Circulation

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The problem of increasing blood flow through an extremity with vascular impairment is a very complicated one and is influenced by many factors. The selection of appropriate therapeutic measures (physical, pharmacological and surgical) is dependent upon the basic disease process. The amount of functional disturbance does not always parallel the degree of organic alteration in the lumen. Profound symptoms may occur with either no pathological change in the vessel wall, as in Raynaud's disease, or with very slight organic changes, as in multiple small embolizations. These are obviously produced by the effects of secondary vasoconstriction. On the other hand, there may exist complete obliteration of the main arterial pathway, such as follows a saddle embolus, and yet a short time later the state of impairment in circulation may be slight. This sequence can be accounted for by the prompt creation of an adequate collateral circulation. Therefore, the basis for improving circulation depends upon the ability to reestablish the blood flow through the major arterial pathway, the creation of maximum vasodilatation of vessels that have assumed the function of the obliterated pathway (collaterals), and the stimulation of growth of a new collateral circulation.

Both etiological and mechanical factors accounting for the impaired circulation must be considered in the treatment. Therapy is formulated to include those remedies which are capable of influencing the basic disease. When dealing with a case of organic obstruction resulting from thromboarteriosclerosis, the patency of the vessel can be increased very little. The problem becomes one of influencing arterial flow with measures which can control the circulation of the collateral pathways. However, circulatory impairment mainly associated with vasospasm can be influenced by attacking the root of the disturbance, as by sympathectomy. Therefore, the basic approach to such treatment is: (a) the creation of maximum states of vasodilatation, either by suppressing the vasoconstrictor impulses or by stimulating the vasodilator fibers, and (b) by the use of measures designed to protect the limb for a sufficient period of time to permit the development of an adequate collateral circulation. Although surgical treatment is urgently indicated at times, operation may be interdicted because of the condition of the patient, or because of the nature of the disease, or the lack of experienced surgical technique. Occasionally, non-surgical methods may maintain adequate circulation until operative interference is possible. The modalities of improving the circulation are of three types: physical, medical and surgical.

A. Physical Methods of Improving Circulation

The past two decades have witnessed the introduction of various mechanical devices intended to improve the circulation in peripheral vascular diseases and in diseases of the aorta that affect the blood flow to the extremities. It is logical that physical methods should play a significant role in attempts to improve the function of the impaired circulation in cases with mechanical obstruction. An extremity may thus be favorably influenced in an otherwise hopeless situation.

1. *Suction and Pressure.* This procedure consists of placing the involved limb in an hermetically sealed boot in which the environmental atmospheric pressure is alternately reduced and increased. Reid and Herrmann originally introduced this method of passive vascular exercise into this country with the Paeve apparatus. The equipment provides for slow cyclic alterna-

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tions in environmental pressure as follows: 80 mm. of negative pressure for 12 seconds and 20 mm. of positive pressure for three seconds for one hour daily. Landis and Gibbon produced another suction-pressure apparatus with quick alternations of 120 mm. of negative pressure for 25 seconds and 80 mm. of positive pressure for five seconds. Both groups of investigators observed evidences of increased arterial flow in extremities with impaired circulation. They claimed improvement in claudication time, relief from rest pain, and healing of ulcers and gangrene. Although some workers have been able to obtain favorable results, the consensus holds that the method has not secured a definite place in improving the circulation.

2. *Intermittent Venous Occlusion.* Collens and Wilensky developed intermittent venous occlusion therapy in 1937. The apparatus is an automatic unit which produces intermittent periods of venous occlusion. This procedure has a physiological and anatomical basis and is an effective method for improving the peripheral circulation.

The treatment consists of the application of a pneumatic cuff around the thigh of the affected limb which is alternately inflated and deflated. The period of inflation is attended by the development of venous congestion which is equivalent to Bier's "congestive hyperemia." The release of the congesting pressure produces a sudden increase in the rate of arterial flow which is known as Lewis's "reactive hyperemia." By creating alternating periods of congestive and reactive hyperemia, the limb is continuously maintained in a hyperemic state.

Another important physiological basis for the therapeutic value of this modality is related to the role of capillary pressure in fluid exchange. This has been clearly demonstrated by the work of Lewis and Grout and Christian. After the sudden occlusion of a main artery, a drop in hydrostatic capillary pressure occurs below the osmotic pressure of the blood, thus interfering with the normal exchange of fluids between capillary and tissue cell. Landis observed that venous congestion is attended by an increase in capillary pressure which appears to manifest itself during the phase of reactive hyperemia. Thus, a method which is capable of increasing capillary pressure above osmotic pressure and which facilitates the exchange of fluids between capillary and cell, must improve the nutrition of the tissues. The treatment is contraindicated when wet gangrene intervenes.

3. *Oscillating Bed.* Sanders devised a bed equipped with a motor and tilting device which alternately elevates and lowers the head and foot of the bed. The apparatus was originally recommended in the treatment of congestive heart failure as well as in peripheral vascular disease. So far as the peripheral arterial disorders and aortic occlusions are concerned, this automatic tilting apparatus accomplishes the same thing as Buerger excercises with the advantage of continuous application of therapy by passive methods. It is of great value especially in saddle occlusions when operation is interdicted.

4. *Whirlpool Baths.* Such baths prepare the way for massage and passive movements. In addition, the hydromassage and increased temperature of the water produce extreme vasodilatation. They also promote lymph circulation and hasten the recovery from sub-inflammatory conditions. The apparatus is devised to maintain an extremity in a rotary water current which can be kept at any desired constant temperature by a regulating thermostat.

5. *Diathermy and Short Wave Therapy.* These forms of heat will be found of value provided they are used with caution. They should be employed within the limits of the patient's comfort, and the patient should experience a sensation of mild warmth rather than heat. Plethysmographic investigations have revealed excellent vasodilator effects from the application of short wave therapy. Of course the electrodes are never placed over the extremity itself. Rather, the heat is centered over the lower spine or other distant region in order to induce reflex peripheral vasodilation without directly increasing the metabolism of the affected limb. Heat applied directly to a limb with impaired circulation may precipitate an impending gangrene. The work

of many investigators has proven the beneficial effects that follow the application of heat to a region remote from the affected extremity.

6. *X-Ray Irradiation.* This has been employed as a conservative method for interrupting the flow of sympathetic impulses. Phillips and Tunick first recommended x-ray therapy to the lumbar spine in an effort to influence the lumbar syspathetic ganglia. They reported excellent results in the relief of pain and intermittent claudication. Pfahler found that small doses of irradiation over the sympathetic ganglia produced significant vasodilating effects. He believed that this procedure is as beneficial as lumbar sympathectomy. A trial of x-ray irradiation over the lumbar region may be of value in cases with a marked vasospastic element as the main factor in circulatory impairment.

7. *Miscellaneous.* There are several other physical modalities of treatment which are popular with individual groups. These include various types of baths, massage, phototherapy, postural exercises, mercury baths, mecholyl iontophoresis and hyperthermia. Each has its adherents, but general acceptance has not been forthcoming in each case.

B. Medical Methods of Improving Circulation

These methods act mainly by way of reducing vasospastic tone and creating vasodilatation.

1. Although intravenous injections of *hypertonic salt solutions* may be of value in some cases of thromboangiitis obliterans and thrombo-arteriosclerosis, their use is not universally recommended. The therapeutic value of this measure lies in the increased blood volume which elevates the filtration pressure in capillaries. However, it is definitely contraindicated in hypertension and arteriosclerotic heart disease since sudden increases in blood volume may precipitate an attack of heart failure and because of the harmfulness of the sodium ion in these states. More recently there has been a marked tendency to desert this form of treatment by many who believe that it has no true physiologic basis.

2. *Intravenous typhoid vaccine* as a nonspecific protein therapy is too hazardous a procedure to be employed in elderly patients suffering from advanced arteriosclerosis. Ordinarily it is an excellent vasodilator, but the shocking effect of the therapy may result in excessive cardiac strain. The treatment demands hospitalization and constant attendance.

3. The introduction of *extracts of various tissues* for the treatment of obliterative arterial disease has proved disappointing. Several preparations have been recommended, the most popular of which is an insulin-free, deproteinated extract of the pancreas commercially known as depropanex. The original reports contended that intramuscular injections improved rest pain and intermittent claudication in arteriosclerosis obliterans. This observation was completely refuted by the careful studies of Dreisbach and associates, who showed that depropanex and padutin, another pancreatic preparation, were incapable of creating antispasmodic effects on smooth muscle even when 400 times the calculated clinical dose was employed. Collens *et al.* evaluated depropanex in a long and extensive trial and discarded it because it was not found to have any demonstrable therapeutic merit.

4. *Alcoholic Beverages.* The vasodilating effect of alcohol is well known. One ounce of whiskey four times a day may be prescribed.

5. *Acetylsalicylic Acid.* This is an inexpensive yet effective vasodilating drug. Bierman studied the effects of various drugs upon the surface temperature in the extremities, a rise in temperature obviously indicating an increased circulation to a part. He found an effective increase in skin temperature following the administration of acetylsalicylic acid. This drug is also advantageous because of its analgesic action.

6. *Papaverine Hydrochloride.* This preparation is of great value in relaxing the reflex vasospastic state of acute thrombosis and embolus of the major arteries and also in controlling pain. In sudden arterial occlusions, it should be given in one-half to one grain doses intravenously every two

to three hours for at least 24 hours. Subsequently, oral administration may be substituted. However, according to Denk, if there is no relief following the second injection, none may be expected with further doses.

7. *Choline Derivatives.* Carbaminylcholine (doryl or lentin) or acetyl beta-metheylcholine chloride (mecholyl) are very powerful vasodilators. Goldsmith believed that mecholyl stimulated the parasympathetic system. Schwab and his associates showed that it also produced local vasodilatation by the inhibition of the sympathetic constrictors. These preparations have dubious value in organic occlusive diseases except in some cases with a large element of vasospasm. Starr emphasized the fact that the side actions of doryl were severe enough to warrant its use with caution in cases where the drug would seem to be of benefit. Mecholyl may be given orally or subcutaneously in doses of 50 mg. three or four times a week. Its action has been known to last from one to six hours. When given subcutaneously, the side actions may be extremely disagreeable. They are characterized by tachycardia, sweating, salivation, nausea and sometimes collapse. Mecholyl produces fewer constitutional effects and more pronounced local action when introduced directly into the diseased part by iontophoresis.

8. *Theobromine and Its Derivatives.* The xanthines have been recommended because of their vasodilator actions. Scupham has noted relief of rest pain and improvement in intermittent claudication. It is generally believed that these drugs are very feeble vasodilators and are without striking benefits even after long use. Theobromine sodium salicylate may be tried in doses of 15 grains three times daily. Aminophyllin (three grains) may also be prescribed three times a day.

9. *Tetraethylammonium Salts.* These have recently been re-introduced and show great promise, both therapeutically and diagnostically, in the treatment of a number of peripheral vascular diseases, hypertension and other disorders in which peripheral circulation is disturbed. They erect a barrier against vasoconstrictor impulses. Clinical investigations of the tetraethylammonium ion have utilized both its chloride and bromide salts. However, as supplies of the chloride became more available for experimental use, this became the form most generally employed. Pharmacological characteristics apply equally well to both salts, but use of the chloride avoids the possibility of bromism. Etamon is the name of a commercial preparation commonly employed.

The drug acts by partially blocking the transmission of both sympathetic and parasympathetic nerve motor impulses through autonomic ganglia. The interruption of sympathetic stimuli associated with vasospasm usually results in an increase in blood supply to the affected extremity as measured by changes in skin temperatures or by plethysmokymography. A reduction in arterial pressure occurs due to the vasodilator effect produced. Therefore, it may be utilized instead of paravertebral or local nerve block in the selection of cases of peripheral vascular disease which are suitable for sympathectomy. It may be given in doses of one to five cc. intravenously, but not to exceed seven mg. per Kg. of body weight; and in intramuscular injections of 10 to 12 cc. (five to six cc. in each buttock), but not exceeding 20 mg. per Kg. of body weight. Frequency of injection will depend upon the duration of relief from symptoms. It may be administered as frequently as once or twice daily. Unfavorable reactions may be relieved with neostigmine or adrenalin because of their antagonizing effects. These include dyspnea, weakness, fatigue, lightheadedness, and difficulty with muscle movement which does not result in impairment of the deep reflexes. Peripheral circulatory collapse has been observed in some patients following intravenous injection, but this is usually transient.

10. *Priscol* (Benzyl-imidazoline hydrochloride). This preparation (25 to 75 mg. doses) improves the circulation by dilatation of blood vessels. The drug acts in three ways: it has a histamine-like effect upon smaller blood vessels; it blocks the augmentor sympathetic vascular receptors; and has an adrenolytic effect which also results in dilatation of blood vessels. It is in the experimental stage at present

but numerous reports have shown favorable results. It has also lowered blood pressure in many cases with higher dosages (100 to 200 mg.).

11. *Anticoagulants* (heparin and dicumarol) are most valuable in some phases of obliterative diseases. These include thrombi, emboli, trench foot and operative repair of blood vessels and other vascular surgery. Their usage is universally established, especially in reducing the incidence of impending gangrene.

12. *Antibiotics* are of vital importance in the control of local infective complications or intercurrent infections. Their use in such conditions as diabetic gangrene, lymphangitis and subacute bactrial endocarditis has been one of the significant advances in modern medicine. The sulfa group may be similarly employed.

C. Surgical Methods of Improving Circulation

Surgery no longer deals with the mere technique of amputation, but has developed methods for improving circulatory efficiency. Its effect on the interrelationship of the sympathetic nervous system and peripheral vascular disease has been well established. Proper selection of patients and adequate sympathetic denervation are most important for adequate results. The effect of sympathectomies in removing the vasospastic element of Raynaud's disease and organic obliterative vascular disease is usually advocated for the following purposes: (1) relief of pain and improvement of collateral circulation, (2) avoidance or postponement of amputation, (3) extending the safe level in cases of inevitable amputation and (4) simplicity and ease of performance.

Operations employed in appropriate cases of peripheral vascular disease include: thoracic and lumbar sympathetic ganglionectomy and ramisection, embolectomy, thrombectomy, aneurysmectomy, peri-aortic and peri-arterial stripping, aortectomy for coarctation, repair of arteriovenous shunts, and repair of aortic and arterial tears or injuries. Methods for alleviating pain include peripheral nerve section, paravertebral block, intraspinal injection of alcohol and cordotomy.

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CASE REPORTS

Agnogenic Myeloid Metaplasia of the Spleen

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Agnogenic Myeloid Metaplasia of the Spleen was first described in this country by Jackson, Parker and Lemon, in the *New England Journal of Medicine* (1940). Agnogenic is derived from the Greek meaning of unknown or uncertain etiology (idiopathic).

This is a syndrome simulating myelogenous leukemia characterized by:

1. Slowly progressive enlargement of spleen.
2. Blood picture simulates myeloid leukemia or acquired hemolytic jaundice.

Hickling says the diagnosis depends on finding immature red and white cells in the circulating blood without a great increase in the total leukocytes in a patient with massive enlargement of spleen.

PATHOLOGY:

1) The spleen shows more or less marked fibrosis with isolated foci of myelocytes and other early forms of the granulocytic series. Also nucleated reds and megakaryocytes are found often in large numbers and malpighian corpuscles are often present. In contrast, the spleen of leukemia shows a marked diffuse infiltration of immature cells of the granulocytic series and malpighian corpuscles are as a rule completely obliterated and infarcts are common. 2) Nucleated RBC are found almost constantly in peripheral blood. 3) Platelets may be increased, normal or decreased. 4) There may be slight jaundice present. 5) Generalized lymphadenopathy does not occur, as there seems to be a failure of bone marrow to form blood and function is taken over by the spleen. The bone marow may be normal, fibrotic, fatty or hyperplastic, therefore these findings are uncertain. Spienectomy and x-ray are contraindicated. There have been sixteen cases of this disease reported by Jackson, Parker and Lemon.

Case Report:

This case, a 68-year-old female, was admitted to the hospital in November 1946, because of weakness and loss of weight from six months to a year. Former weight 167 pounds; weight on admission 135 pounds. She had been seen by local M.D.'s in the past two to three years for arthritis of both knees and hip. No pain, vomiting or melena. No bleeding from skin or mucous membrane.

HISTORY:

Past and family history noncontributory.

Physical Examination:

Patient shows evidence of weight loss, skin dry, not acutely ill. Glands negative, chest clear, heart not enlarged, no murmurs. BP 150/80. Abdomen protuberant and hard, not tender. Liver hard and smooth, one hand's breadth below costal margin. Spleen firm, smooth and felt right down to iliac crest.

BLOOD: November 1946.

Examination of Blood revealed:

RBC	3,780,000
WBC	7,100
Hb	78.7%
	12.1 gm.
Myelocytes	4
Metamyelocytes	6
Stabs	32
Segmented	26
Total	68
Lymphocytes	29
Monocytes	0
Eosinophils	0
Basophils	3

Read before the Scientific Session of the Associated Physicians of Long Island, held June 15, 1948, at the North Country Community Hospital, Glen Cove, N. Y.

Remarks: Blood smear showed a marked anisocytosis, with a moderate number of normoblasts, microcytes and poikilocytes; also many polychromatic erythrocytes and many erythrocytes with basophilic stippling.

May 22, 1947 examination of blood revealed:

RBC	4,180,000
WBC	10,850
Hb	66%
Basophils	2
Juve.	13
Myelo.	17
Stabs	25
Lymph.	16
Anisocytosis	
Polychromatosis	
Megakaryocytes	10
Stippling	

March 19, 1948 Blood examination revealed:

RBC	4,470,000
WBC	15,000
Hb	74%
Poly.	45
Lymph.	55%
(20% Pathological)	

BONE MARROW aspiration by Dr. Leo Meyers on May 27, 1947:

Total nucleated cells 35,000
Megakaryocytes 3 per chamber field
Segmented Basophils 1.5%
Segmented Neutrophils 13.5%
Segmented Eosinophils 0.5%
Non-segmented Eosinophils 14%
Normoblasts 39%
Retic. Endothel. cells 1%

Note by Dr. Meyers: The above precludes a diagnosis of myeloid leukemia because of the hypoplastic granulocytic elements. The lymphocytosis and normoblastosis reflect only a relative hyperplasia which is not absolute. Probable diagnosis: Agnogenic Myeloid Metaplasia.

Fragility Tests: May 27, 1947 Beginning Hemolysis .46%; March 20 1948 .46%; Complete Hemolysis .38% .32%

Platelets May 27, 1948 356,000 and March 19, 1948 152,000

Hematocrit 33 cc. and Reticulocytes 7.4% March 19, 1948.

Sedimentation Rate 14 May 1947.

Bromsulfalein 5% after 30 minutes.

Icteric Index

	May 20, 1947	March 20, 1948
Icteric Index	4.4	3.0
Total Protein	6.5%	7.1%
Alb.	4.4	4.6
Glob.	2 .1	3.2

Sugar 94

Serum Bilirubin .1%

Alk. Phosphates 7 units.

Hanger 3 plus after 48 hours.

Urine Sp. Gr. 1.010, occasional WBC, Albumin trace.

X-RAYS, LONG BONES, May 23, 1947.

Films to show the entire vertebral column in AP projection, from the level of T7 to the coccyx, demonstrate a ground-glass appearance of all of the vertebral bodies. The normal trabecular structure cannot be made out. No definite sclerotic change. Films of both humeri, radius, and ulna together with films to show entire tibia and fibula fail to demonstrate conclusive x-ray evidence of bone abnormality. It is possible that the ground-glass appearance of vertebrae is the result of hyperplastic changes in the trabeculi. Hyperplastic osteoid tissues in the absence of mineralization could give this appearance.

May 1947, CHEST: No definite x-ray evidence of abnormality of heart or lungs. March 20, 1948: Films to show esophagus during the administration of barium by mouth, and fluoroscopic examination, fail to show evidence of esophageal varices.

A diagnosis of Agnogenic Myeloid Metaplasia of the Spleen was made on the basis of Jackson's classification of a slowly progressive enlargement of the spleen, simulating myeloid leukemia, and the finding of immature red and white cells in the circulating blood, without a great increase in the total leukocytes; generalized lymphadenopathy does not occur.

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The Use of an Antispasmodic Combination in Various Medical Conditions

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An antispasmodic combination consisting of extract of belladonna leaves, 11 mg., homatropine methyl bromide 2 mg. and phenobarbital 16 mg. per tablet* was used in a series of 66 cases comprising various medical conditions where relaxation of smooth muscles or depression of the vagus or both simultaneously were deemed advisable. The results were highly satisfactory.

Pathology of Spasm

Bernstein and Brenner[1], in discussing neuro-functional spasm, state that spasm of some part of the alimentary tract from the pharynx to the rectum is a common cause for the patient's discomfort. It may occur in children or adults; it may involve one or more sphincters or areas at one time. Physiologically, spasm is caused by either an intermittent or constant stimulation of a motor nerve, causing the muscle fibers which it supplies to contract for a variable period of time. Spasm is clonic if brief and intermittent or tonic if prolonged. Spasm manifests itself either by retention of content proximal to the point of action with its resultant symptoms of eructation, heartburn, belching, nausea or vomiting, or more frequently and forcefully, by pain. The actual impulse responsible for setting up efferent stimuli from the alimentary tract is apparently a local smooth muscle tension secondary to a local distention of the tube or its equivalent: an abnormal constriction called increased tonus or spasm. Spasm may be the result of a local organic lesion such as esophagitis or appendicitis or proctitis. It may be of reflex origin, the cause being remote from the location of the phenomenon. Finally, it may be of functional or psychosomatic origin.

Pharmacology of Antispasmodic Drugs

Sollmann[2] states that the atropine-containing durgs such as belladonna have long been used against spasm of the smooth muscles, ranging from asthma to the various "colics". They are highly successful in the cases where the spasm is due to parasympathetic stimulation. Several derivatives of atropine have been introduced as antispasmodics with the claimed advantages of fewer side actions on other functions. Among these is *homatropine methyl bromide* which is used especially against gastro-intestinal spasm and hyperchlorhydria. It is less toxic and less potent than atropine. Cushny[3] regards its toxicity as compared with atropine as 1:33.

Gold[4] agrees that the atropine group acts by blocking the functions of the parasympathetic. He explains the fact that it frequently relieves pain in the gastro-intestinal tract by the fact that it diminishes the tone and motility of the stomach. It may take as much as four times as long as normal for barium to appear in the duodenum and two and a half times as long as normal for the stomach to rid itself of the barium completely. The diminished motility may result in lower tension in the stomach even though the spasm may be uninfluenced. Similar diminution in motor activity of small intestine or colon has been observed after giving suitable doses of atropine.

Goodman and Gilman[5] assert that although it is commonly stated that ordinary therapeutic doses of belladonna alkaloids have no significant influence upon normal peristalsis, intubation studies combined with fluoroscopy in normal subjects in-

* The medication referred to in this article is known as Amalgin and is manufactured by the Amfre Drug Company, Inc., 95 Madison Avenue, New York 16, N. Y.

dicate that clinical doses of atropine sulfate and tincture of belladonna produce definite and prolonged effects on the motor activity of the duodenum, jejunum, ileum and colon, consisting of a marked decrease in the tone and in peristaltic movement and of a less striking effect on rhythmical contractions (Elcan and Drossner[6]. Jackson and Gargen[7]).

Conditions Where Antispasmodics Have Been Found Useful

Peptic ulcer.—It is a well established fact that there is a marked psychosomatic element in peptic ulcer. Fredenhagen[8] studied a series of cases of gastric and duodenal ulcers. Symptoms of vagotonia were observed more frequently than symptons of sympathicotonia. The vagotonia was most pronounced in patients with duodenal ulcers and with recurrences of chronic ulcers. Vagotonia did not decrease with a higher age.

Cox and Juannila[9] in a study of 161 naval enlisted men found that 83 had a history of ulcer established by x-ray when admitted or before admission; 78 of the group also had anxiety neurosis or combat or operations fatigue. Treatment consisted of ulcer diet, belladonna, phenobarbital, antacids and psychotherapy.

Kirsner and Palmer[10] found that atropine was very useful in the treatment of peptic ulcer, its action being ascribed to prolongation of the gastric emptying time as well as its reduction of the volume of gastric secretion.

Parson[11] emphasizes the importance of rest of body and mind in the treatment of duodenal ulcer. He states that the tense, nervous or apprehensive person should receive some form of barbiturate. He adds that antispasmodics such as belladonna and atropine are often serviceable.

Weintraub[12] advocates a combination of phenobarbital and extract of belladonna in the treatment of peptic ulcer. He states that this combination has both a sedative and antispasmodic effect. Even though the dose of belladona is small, it has been observed that most patients show that the drug is effective.

Holland[13] states that atropine and belladonna stand out as the principal agents that we employ as antispasmodics in the treatment of peptic ulcer. He states that these agents seem to establish a better balance between the vagus and sympathetics which has something to do with quieting and regulating the peristalsis of the gastro-intestinal canal.

Boles[14] feels that the term "peptic ulcer" should be abolished and the condition should be named "neurocirculatory ulcer." He states that while it is a well established fact that measures designed to diminish the secretion of acid provide comfort for the patient, it must be remembered that these same measures allay pylorospasm and that this may account for their effectiveness.

Pylorospasm and cardiospasm.—Thompson[15] attests the usefulness of belladonna derivatives in pyloric stenosis from spasm and edema but not in cicatricial stenosis.

Sollmann[2] states that pylorospasm and cardiospasm are relieved by belladonna compounds if due to vagus stimulation but not if they are of sympathetic, emotional or ulcerative conditions. Other writers differ from Sollmann in the last two conditions.

Piersol[16] asserts that the drug which tends to relieve spasm of the pylorus better than any other is atropine.

Goodman and Gilman[5] tell us that pylorospasm or cardiospasm may be lessened or abolished by atropine.

Beckman[17] states that during an acute attack of pylorospasm, atropine gives complete relief. Even infants tolerate relatively large doses (0.8 to 2.4 mg.) with no significant reactions.

Morrissey[18] mentions seven cases of cardiospasm treated by atropine plus atropine derivatives with added phenobarbital.

Biliary colic.—Bockus[16], in discussing biliary colic, states that it is possible that if patients were instructed to use an anti spasmodic with the advent of the earliest warning of a pain attack, severe "colic" might be prevented in some instances. Quite often relatively mild discomfort is experienced in the epigastrium from one half to two hours before the more severe pain occurs. Atropine may be tried dur-

ing the incipient stage of a subsequent attack. If it proves successful in aborting a severe attack of "colic," it should be available at all times and utilized by the patient when the first indication of a return of slight pain presents itself. Unfortunately most often relief is not sought until the pain has become sereve or intolerable. At this stage, antispasmodics alone rarely relieve the pain and opiates combined with atropine may be required.

Sollmann[2] attests the usefulness of atropine in biliary colic (as well as in renal colic), stating that it paralyzes the smooth muscles of the bile ducts (or ureters) and therefore relaxes the painful and obstructive spasm which results from the passage of calculi through these tubes. The vagus paralysis is useful by preventing the dangerous cardiac reflex which sometimes occurs.

Renal colic. — Morrissey[18] states that since the advent of the sulfonamides, penicillin and streptomycin, there has been a general tendency toward conservatism in the treatment of ureteral calculi. This trend is due not only to the knowledge that a large proportion of ureteral calculi pass spontaneously but to the less formidable nature of the renal complications resulting from the conservative treatment of obstruction now that we possess such a potent chemotherapeutic armamentarium. He goes on to state that the fact that the motor innervation of the ureter is of sympathetic origin while that of the bladder detrusor is at least predominantly of parasympathetic origin, seems momentarily to offer an impasse to the rationale of treatment of bladder muscle spasm and ureteral muscle spasm with the same group of drugs. But to quote from Henderson and Roepke[20]: "The purely anatomical division of the autonomic nerves into sympathetic and parasympathetic is pharmacologically meaningless . . . at all events as far as concerns the characteristics of the postganglionic fibers. . . . It is evident that atropine diminishes or in higher concentrations prevents the normal effect of nerve stimulation in the case of all parasympathetic and many sympathetic endings. . . . The successful relief of ureteral spasm not only diminishes or abolishes pain but in the case of ureteral calculus may actually facilitate the spontaneous passage of the stone. . . ."

Morrissey[18] used a combination of atropine with other belladonna derivatives and phenobarbital in 37 cases of renal and ureteral colic due to stone and in 69 cases of colic due to obstruction and found the combination of drugs to be most effective therapy for the relief of pain and spasm with amelioration occurring in the greater proportion of cases within a 36 hours period.

Constipation, colon consciousness, irritable colon, unstable colon, spastic colitis. —Bockus[19] has emphasized that functional disorders of the colon are one of the disorders of civilization. They are common in the more emotional races or among the so-called "sentimental stock." Fatigue as well as nervous stress and strain often is provocative of attacks in susceptible persons and upper respiratory infections may cause an acute exacerbation of symptoms.

Bargen[21] states the following: "Our present day life with its hustle and bustle, its tremendous competition in wage earnings and its every urge for speed, often interferes with proper care of intestinal function. There results therefore a 'nervous indigestion' in which the colon plays no small part. After a morning rush to the office, there is often an all day rush in a highly competitive business. A person does not have time to stop for evacuation of the bowel. There is improper intake of fluids, the noonday meal is eaten hurriedly and under the most adverse conditions. At night, such a person probably eats his dinner hurriedly to prepare for the evening activities. He retires late only to arise again improperly rested to go through the same procedures as on the previous days."

Collins[22] gives a report on 1,000 cases of irritable colon. In most instances, there was a long history of recurrent bouts of abdominal discomfort related to irregular bowel habits. The intensity of the distress varied, the most familiar example of severe intestinal colic being the well-known "green apple belly ache" of childhood. When the distress is severe, the symptoms

are similar to those of chronic ulcerative colitis, diverticulitis of the sigmoid colon, or may simulate biliary or renal colic. Usually the distress varies from a shifting cramp-like pain to a sense of fulness often associated with gaseous dyspepsia; i.e., abdominal distention, rumbling and gurgling, belching and excessive flatus. Constipation, diarrhea or normal bowel movement may be present. There may be large amounts of mucus or mucous casts. The distress is most marked during the periods of greatest activity. The treatment consists of rest and non-residue diet followed by high protein, high carbohydrate, low residue diet. Antispasmodics and mild sedatives are given one half to one hour before meals.

Chronic nonspecific ulcerative colitis.—Kirsner, Palmer, Maimon and Ricketts[23] report on a study of 100 cases of nonspecific ulcerative colitis. The symptoms consisted of bloody diarrhea, rectal tenesmus, fever, anorexia and weakness. Definite psychogenic factors were present in 67 cases. The patients often were described by the psychiatrists as immature, dependent and overtly passive. Anxiety states, insecurity, hostility, sexual maladjustments and schizoid tendencies were commonly observed. There was a tendency for the symptoms to recur or to become accentuated during the development of situations requiring responsible and decisive action; 81 cases were treated medically and 19 surgically. The medical treatment consisted of bed rest, sedatives and antispasmodics, psychotherapy and a bland, nutritious diet. Of those medically treated, there was slight improvement in 19, none of whom were significantly incapacitated, moderate improvement in 25, apparent cure in 6 and 9 deaths.

Coronary and certain other heart conditions.—Gilbert[24] gives atropine routinely in all cases of recent coronary occlusion, the theory being that reflex vasoconstriction of the arteries in the uninvolved heart muscle is thus counteracted. The same author in another article[25] states that those patients convalescing from coronary occlusion as well as those subject to angina pectoris are placed upon a strict routine. Full heavy meals and gas forming foods are avoided. Great stress is laid upon the fact that the patient should approach the taking of a meal in as calm and relaxed a condition as possible. A small dose of belladonna or phenobarbital at meal times is a great help.

Weiss and English[26] state the following: "The neurotic patient who has organic heart disease may add a real burden to the work of his heart either through constant tension of psychic origin or more especially by means of acute episodes of emotional origin. This may hasten a cardiac breakdown which might be indefinitely postponed if there were no psychic stress." These findings substantiate the logic of using antispasmodics (belladonna or homatropine methyl bromide) plus sedatives (phenobarbital).

Carell and Lindert[27] report the successful use of homatropine methyl bromide in a man in the seventh decade suffering from the type of heart block known as Stokes-Adams disease.

Goodman and Gilman[5] state that atropine is occasionally of some value in the treatment of premature systoles. It is also serviceable in a patient experiencing bradycardia or complete systolic arrest with syncope as a result of an abnormally active carotid sinus. Weiss and associates[28] have shown that therapeutic doses of atropine abolish the vagal type of syncope in patients with hyperactive sinus mechanisms.

Bronchial asthma.—Belladonna derivatives are not to be considered the main drugs in the treatment of most cases of bronchial asthma. Epinephrine or ephedrine are the most effective drugs in most cases. However, Sollmann[2] states that atropine is useful as an adjuvant to epinephrine. Piersol[16] states that the occasional asthmatic patient responds brilliantly to atropine.

Certain types of bronchitic.—Cushny[3] asserts that atropine is of value in bronchitis with excessive secretion.

Paralysis agitans.—Sollmann[2] attests the usefulness of atropine in Parkinson's syndrome, stating that it is useful against muscular rigidities in such cases, especi-

ally when following encephalitis, often with considerable relief of the muscular stiffness, disturbance of speech and writing, the tics and salivation and causing improvement of the restlessness and depression but with little improvement of the psychoses and tremor. Piersol[16] likewise states that in paralysis agitans and postencephalitic parkinsonism, therapy with belladonna alkaloids is one of the few measures that offers some measure of symptomatic relief. A majority of patients experience improvement after these drugs are given. Tremor, muscular rigidity, abnormal gait, speech and posture, oculogyric crises, dysphagia, hyperhidrosis and sialorrhea respond favorably and consequently the mental outlook often improves. Treatment is purely palliative and the course of the disease is not altered.

Dysmenorrhea.—Sollmann[2] informs us that atropine in dysmenorrhea was advocated by Novak in 1915, especially in the spasmodic type. Marchetti[29] advocates atropine for dysmenorrhea stating that it brings about relaxation of the smooth muscles. It helps especially, he states, in patients with hypoplastic uteri. Beckman[17] states that in the experience of most physicians who use atropine or some other member of the belladonna series—and nearly all do for there is occasionally a strikingly good result—the colicky pains are much more relieved than are the backache, bearing down in the lower abdomen, lassitude, etc.

Novak[30] stresses the psychogenic factors of dysmenorrhea. He states that while many women suffer no discomfort whatever during menstruation, a moderate amount of pelvic heaviness and even an occasional cramp may be considered within normal limits. Indeed, the line between this

TABLE I

The Results of Amalgin Therapy in a Series of 66 Cases

Diagnosis	Number of Cases	Number with Complete Remission	Remarks
Biliary Colic	5	4	1 complicated by stones
Pylorospasm and Cardiospasm	9	7	1 malignancy—1 other
Peptic Ulcer*	22	16	4 obtained temporary relief —2 required surgery
Bronchial Asthma	5	5	2 complicated by emphysema
Coronary Sclerosis and Angina Pectoris (No cases of thrombosis)	4	4	- - - - - - - -
Constipation, Colon Consciousness, Spastic Colitis and Non-sepcific Ulcerative Colitis*	12	11	1 case of nonspecific ulcerative colitis obtained some relief. Surgery recommended
Renal Colic	6	6	Uncomplicated cases such as Dietl's crisis. Stones not found
Paralysis Agitans	3	Partial Remission in 3	Marked improvement of symptoms, tremor appreciably decreased, gait improved

* Plus diet, vitamin therapy and fluid increase in colitis series; antacids, diet, vitamin therapy and fluid regulation in ulcer series.

normal discomfort and real dysmenorrhea is a very shadowy one and the distinction is commonly made subjectively by the patient herself on the basis of the incapacity produced. It is this subjective nature of the disorder which has made its study so difficult. It needs no more than a knowledge of human nature to justify the statement that the same degree of peripheral stimulus which in the well balanced, phlegmatic individual will be expressed as a moderate discomfort, will manifest itself in the high-strung supersensitive girl by severe and perhaps incapacitating pains. The psychogenic element therefore is one which can never be lost sight of in the management of cases of dysmenorrhea and a comprehensive study includes a consideration of factors which may accentuate the subjective element in the particular case. Among these are a congenitally unstable and high-strung nervous system, psychic trauma, especially when related to the menstrual periods, and wrong ideas as to the significance and normality of the menstrual function. This last named factor is frequently encountered. Many a young girl at the beginning of her menstrual life is coddled by an overly anxious mother into the belief that menstruation is a time when she should really consider herself "unwell." To such a girl, especially if reared in a household where one or more others among the female members suffer from dysmenorrhea, the transition to menstrual invalidism is a very easy one. So important are these possible factors that there are some authorities who assert that the cause of primary dysmenorrhea is invariably psychogenic, a view which Novak does not share. On the other hand, he is convinced of the prime role of the psychogenic factor in many cases.

Crossen and Crossen[31] likewise stress neurogenic factors in dysmenorrhea. They state the neurogenic factors causing dysmenorrhea have been investigated by Kieffer. He found that stimulation of the internal os caused uterine contractions, cervical spasm and pain. From his study he concluded that the cervix was a spincter with its tone governed by a reflex arc through the lumbar cord and the cervical ganglia of Frankenbauer. Kieffer feels that the spasmodic pain experienced in cases of dysmenorrhea may be due to an abnormal state of the cervical ganglia. This theory has received support from the practical work of Blos and also Kennedy. Crossen and Crossen add that atropine has been used with relief in some cases.

Caution.—Belladonna derivatives should never be used in the presence of glaucoma.

Case Reports

A series of 66 medical cases of various types was given the antispasmodic-sedative combination named early in this article. The cases of renal and biliary colic were given two tablets every four hours until the symptoms abated—a period varying from two to five days. The other cases were given one tablet every four hours for a period of 90 days. The medication was then discontinued in all but the cardiac cases, who were given a maintenance dose of one tablet three times daily thereafter for an indefinite period.

Comment

In a series of 66 cases of various types of medical conditions treated by the antispasmodic and sedative combination known as Amalgin, 53 (80.3 per cent) showed complete remission and 60 (90.9 per cent) showed great improvement. These results have been highly gratifying.

Summary and Conclusions

1. The pathology of spasm and the general theory of the use of antispasmodics has been discussed.

2. A variety of conditions that have responded favorably to antispasmodic therapy has been enumerated.

3. A series of 66 cases treated by means of an antispasmodic and sedative combination known as Amalgin and consisting of extract of belladonna, homatropine methyl bromide and phenobarbital has been reported.

4. The results have been most favorable in the vast majority of cases.

5. The use of the above named combination in conditions requiring antispasmodic therapy has been proven to be both logical and effective.

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145 West 71st Street

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THE PROBLEM OF THE SEXUAL OFFENDER

—Concluded from page 28

ment and not to expect life to be always pleasurable and to revolve only for their comfort.

Although some psychiatric help can be offered to many offenders, the great hope lies in prevention, rather than cure. Such prevention, by the indoctrination of the parents, will aid them in rearing children who may learn to shoulder the responsibilities of adulthood and make them attain a happier and better adjusted adult life. The community responsibility is obvious, for only by producing mature, contented citizens can it hope to cope with many of its social problems.

1850 South Avenue.

METHODS OF IMPROVING THE PERIPHERAL CIRCULATION

—Concluded from page 33

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EDITORIALS

It Might Just As Well Be a Hoax

Why is it that demands are being made upon our government that can not be honestly met? Even the priority of military defense is currently challenged by compulsory sickness insurance's preposterous proposal. Can it be that this particular proposal is a hoax and its proponents humorists of a new type trying to see how far a practical joke on the country can be carried out? The cost would be prohibitive, a low quality of medical care would be offered, the social order distorted and degraded, and medicine itself and its directly and indirectly involved practitioners debased. After such a debauch there would be no return to former (present day) standards.

The ruinous burden on the national economy inherent in the Washington Administration's plans is just funny to read about; but its possible emergence into fact at the hands of smug bureaucrats seems incredible.

Perhaps the American humorist, for so long under protracted strain, is psychiatrically taking a sardonic turn to the left.

If we are to be hoaxed we shall deserve it.

It may not be a hoax but it could be—might just as well be!

Epidemiology of Yellow Fever (1949 Type)

Nationalized medicine is like an infectious disease with epidemic possibilities.

Our job in 1949 and thereafter is to quarantine it, just as we used to deal with yellow fever in this country in former years.

This modern sickness was forcefully characterized in September, 1948 by Dr. Melchior Palyi, "probably one of the three highest ranking economists in the world," in the course of his remarks before the National Conference of the Professions in Chicago: "Great Britain," he said, "has adopted the German system of Socialized Medicine. The operation of the plan will produce practically suicidal deficits. Under the French system, the public gets free service. The physician gets minimum fees as a result of which the doctors have no time for individual patients. An army of bureaucrats is required to check the doctors and check the patients and other bureaucrats to check all these. *The operation results in a peculiar type of legalized corruption which eventually will lead to National bankruptcy.*"

Whenever the old Yellow Jack invaded the United States it was fought vigorously and finally conquered at its source by the Reed-Gorgas group. When the Yellow Jack of 1949 threatens the welfare of the country shall we be any the less ready to crush it? Or have we entered upon degenerate days?

Add Automobile Television to the Moron's Alcoholism

Life (December 6, 1948) informs us that portable television sets have cropped up in automobiles and goes on to say that "Probably a law should be passed right now against putting automobile television sets within the view of the driver—before it is too late."

But the laws on the books looking to the prevention of accidents are already violated on a vast scale. So would be a television law. It's just a matter of fines and insurance.

No laws will change mentalities—and the liquor trade is a legalized industry.

Perhaps the massacre, bizarre feature of a grotesque civilization, will have to continue. Meanwhile hospital "teams" are

prepared for all casualties.

At least the massacre has eugenic connotations.

Puritanism Versus Communism

The puritanic spirit is often held accountable for much of the lure of sexual pleasure. "This attitude creates the psychology of the forbidden fruit. Lifting the ban of convention (within the dictates of ethics and common sense) may make the fruit less tempting . . ." [Benjamin]. To a degree, puritanism implements sex. The opponents of this prohibitionist spirit and alleged consequent repression contend that the neuroses and wars are related to the deprivation or restriction of what they call sexual liberty by what they call senseless taboos.

But many suspect that if the concepts of naughtiness and sin were to be abolished by these conspirators, matters of sex would cease to be so fascinating.

If the anti-puritans, now so much in evidence in one guise or another, were really to succeed in putting down all modesty, chastity, and acceptance of traditional moral codes, would they not defeat themselves? Would not the glamour of sex then prove impotent to excite interest, or rather, would not sex cease to have any glamour? And would it not seem that human beings, having ceased to be reasonably human, would then be ripe for communism, in the sense that their solely biologic and dull lives would lend themselves admirably to a planned apparatus of the State, with a virtually complete sacrifice of erotic interests to the aims of pure materialism? It would be only the wheat index, or the steel production, or the population rate, or the eugenic objectives that would matter—not the individualistic and romantic dreams of any present Jack and Joan.

Add one more to all the other menaces of totalitarianism. The choice seems to lie between puritanism and communism. It may not be the aim of all of our would-be liberators to conditions us for communism; they may mean well, but in setting us "free" in their style these messiahs would be exposing us to a horrid hazard. Incorrigible puritans that we are, and costly as our puritanism is, we cling tenaciously to the way of life that is to our taste.

Puritanism and its neuroses may be the price we have to pay for a qualified freedom.

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EARLY RISING OF PUERPERAE

—Concluded from page 2

Summary

1. Instrumental intervention is not deterrent to early rising unless of a complicated nature.

2. The early risers have a more rapid return to normal body function.

3. Involution of the uterus occurs more rapidly in the early risers than in patients that have had complete bed rest.

4. Early postpartum rising is of economic importance to the patient because it reduces the period of hospital care and disability at home.

105 East Main Street.

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CONTEMPORARY PROGRESS

OTOLOGY

The Feasibility of Group Audiometry

C. K. Myers, J. D. Harris and E. P. Fowler, Jr. *(Industrial Medicine,* 17:245, July 1948) report a group audiometry study of 1,448 young men in a junior college, all veterans of World War II. Three audiometers were used: a Western Electric 6 BP with 24 Permoflux P D R—8 phones in sponge rubber oval cushions giving approximately 24 db attenuation; a Western Electric 6 B with 90 headphones of the same type; and a Maico audiometer with air and bone conduction units for individual testing. The group audiometers were calibrated. Complete audiometry was done on the 1448 men in seven full working days; 39 of these men were given individual tests only and not given group testing; in 11 cases this was due to irregularities in scheduling tests rather than to known deafness. Examination of the six-octave audiograms of the 1409 who were tested by the group procedure showed that a satisfactory audiogram was obtained by this method in 86.5 per cent; 189 men, or 13.5 per cent, were referred for individual testing because the group testing did not give satisfactory results. In this group of 189 men, there were 164 who showed loss of hearing at one or more frequencies greater than the group test could measure; there were, therefore, only 25 men, or 1.8 per cent, for whom the group testing could have given satisfactory results but did not. Of the 189 men referred for the individual test, 40 per cent needed a check up at only one frequency, and 20 per cent at only two frequencies. Pure tone audiometry by the method described can substitute to some extent for the time-consuming individual tests in large population groups. From the results obtained in this study it is concluded that a group method of pure tone audiometry will give accurate results in "a reasonable alert adult population" within a 2 per cent error.

COMMENT

The accuracy of results in such group testing would seem to be satisfactory. Of course, correlation of these results with hearing for speech and its relation to job selection will require further study. ***L.C.McH.***

A Newer Concept of the Management of Otogenic Infection

M. B. Hayes and C. Fremont Hall *(Archives of Otolaryngology,* 47:289, March 1948) report a study of otogenic infections in the last five years, in which they have found that in the temperate zone winter infections are chiefly otitis media due to gram-positive organisms and summer infections are chiefly otitis externa or exacerbations of chronic otitis media due to gram-negative organisms. Acute otitis media due to gram-positive organisms can usually be successfully treated with the sulfonamide drugs and antibiotics with few complications. If otitis media persists and becomes chronic, it will usually be found to be due to a persisting infection with gram-negative organisms, against which these drugs are not effective. External otitis was also found to be due chiefly to gram-negative organisms in the temperate zone, less frequently to fungi. The predominating gram-negative organism in both chronic otitis media and external otitis has been found to be *Pseudomonas aeruginosa (Bacillus pyocyaneus).* In the search for a chemical agent effective against

this type of infection it was found that a new compound, dibromosalicylaldehyde, gave the best results and it was also effective against fungi. Dibromosalicylaldehyde is a crystalline compound with the empiric formula $C_7 H_4 O_2 Br_2$. In cases of chronic otitis media with gram-positive organisms predominating, penicillin was given by intramuscular injection in the usual dosage until the ear became dry or the gram-positive organisms disappeared. If the otitis did not clear up under penicillin treatment, it was found that gram-negative organisms, especially *Ps. aeruginosa*, persisted. These cases were then treated with dibromosalicylaldehyde; a 1 per cent solution of this compound was used for cleansing and irrigation once or twice daily, followed by insufflation of a powder of dibromosalicylaldehyde (2 per cent), sodium borate (3 per cent) and talcum (95 per cent). In the treatment of otitis externa, treatment was begun immediately after the initial culture was obtained. The ear was first cleansed as thoroughly as possible. In cases of otitis externa diffusa, a wick of gause, saturated with "carbowax" containing 2 per cent dibromosalicylaldehyde, was introduced into the ear canal, and allowed to remain for twenty-four to seventy-two hours; this procedure was repeated as necessary. In otitis externa of the eczematous type either the wick was used or a local application for twenty-four hours, followed by dry cleansing and insufflation of the dibromosalicylaldehyde powder, repeated at daily to weekly intervals, as indicated. In 28 cases of chronic otitis media treated with dibromosalicylaldehyde, 12 ears became dry in less than two weeks; 2 cavities following radical mastoidectomy cleared up in less than two weeks; in one case of chronic otitis media with complicating external otitis, complete resolution with healing of the drum occurred. The other cases required treatment for longer periods up to two and a half months, but only 8 failed to clear up completely. In 71 cases of external otitis, 21 acute cases and 30 chronic cases showed complete healing usually in less than a week; 20 chronic cases required longer treatment; of these 3 failed to complete treatment.

COMMENT

A new valuable feature of this article calls our attention to the presence of gram-negative organisms in many ear infections and the necessity of using different medicaments from those used for purely gram-positive infections. The preparation mentioned would seem to be quite satisfactory. ***L.C.McH.***

Therapeutic Evaluation of Iso-Par In Otitis Externa

J. S. Walker (*Bulletin of Johns Hopkins Hospital* 83:225, Sept. 1948) reports the use of Iso-Par in the treatment of 41 cases of otitis externa, 23 of which were acute and 18 chronic. Iso-Par is a mixture of water insoluble isoparaffinic acids partially neutralized with *iso*cytyl hydroxybenzyl-dialiphitic amines; the ointment employed contained 17 per cent of

Iso-Par and 4 per cent of titanium dioxide in a lanolin and petrolatum base. In the treatment of these cases in this series, the ear canal was first carefully cleansed of all debris and discharge with applicators soaked in alcohol, then a thin coating of the ointment was applied. This treatment was repeated as often as necessary in the clinic during the acute phase; and later the patient was instructed in the use of the ointment at home. Heat, aspirin and codeine were employed as supplementary treatment as indicated.

As a rule there was usually definite relief of itching and pain after the first application of the ointment. Some patients required treatment for only five to seven days; others required treatment for as long as two months; for patients with recurrent infections, the prophylactic use of Iso-Par once a week was advised. Of the 41 patients treated and adequately followed up, 25, or 60 per cent, were cured; 10, or 24 per cent, improved; and only 6, or 16 per cent, not improved. No sensitization to Iso-Par was observed.

COMMENT

In our experience very few patients would return if alcohol were used in their ears for acute otitis externa. We are also a little skeptical as to the feasibility of teaching patients to use an ointment in their own ears. Usually after such self medication, we find the canal clogged with the ointment. This seems to be another very useful medicament, especially when used along with meticulous cleansing of the external meatus. ***L.C.McH.***

The Effects of Negative Air Pressure in the Middle Ear

E. G. Wever and associates (*Annals of Otology, Rhinology and Laryngology*, 57:418, June 1948) report a study of the effects of negative air pressure in the middle ear, using cats as experimental animals and determining the electrical potentials of the cochlea to show how the ear's efficiency in sound reception was effected by the changes in air pressure. Similar experiments had previously been carried out on the effect of positive air pressure in the middle ear. Negative air pressure in the middle ear as produced experimentally is similar to that produced by a rapid descent from a high altitude without equalization of pressure in the middle ear. It was found that decrease in the air pressure of the middle ear usually causes a reduction in the electrical responses of the cochlea; the perception of low tones is affected to a greater degree than that of high tones. In some experiments with relatively slight changes in air pressure there was slight improvement in perception of certain higher tones; but when the pressure changes were greater, the perception of these tones was also unfavorably affected. The effects of negative air pressures were found to be very similar to those of positive air pressures as determined in the previous experiments. These experiments have shown that the effects of both positive and negative air pressures in the middle ear are due to the action of the pressure changes on the conductive system of the middle ear, and especially on the ear drum. Either positive or negative pressure displaces the ear drum from its normal position, and increases both the stiffness and the damping of this mechanism. There is also some effect on the inner ear. These studies on the effects of changes of air pressure in the middle ear are of interest in relation to certain clinical observations. For instance in some cases of inflammation in the upper pharynx, the eustachian tube fails to open normally during swallowing, and the usual ventilation of the middle ear cavity is interfered with, resulting in the production of negative pressure in the ear and retraction of the drum. This causes not only a feeling of fullness and discomfort, but usually a definite impairment of hearing. Treatment for this condition involves methods of introducing air into the middle ear cavity by way of the eustachian tube; such treatment may improve the hearing, but often only temporarily.

COMMENT

Some interesting observations regarding effect of negative and positive pressure within the middle ear. A word of caution regarding introducing air into the middle ear by way of the eustachian tube during acute inflammation in the upper pharynx would seem to be in order because of the danger of spreading infection into the middle ear mechanically. ***L.C.McH.***

GYNECOLOGY

The Use of the Vaginal Smear In a Gynecological Service

L. L. Mackenzie and associates (*American Journal of Obstetrics and Gynecology*, 55:821, May 1948) report the use of the vaginal smear technique at the New York Post-Graduate Hospital since 1940. In the series reported the smears were not made as a routine measure, only for the solution of a definite question. The stain devised by Papanicolaou as modified by him has been used most frequently. In a study of smears from menopausal patients, various types were found varying from the early crowded type (showing large numbers of pale-staining superficial cells with large nuclei) to the deep atrophic type. The crowded type of smear predominated in cases of both the normal and the surgical menopause, but the atrophic type was 10 per cent more frequent in the surgical menopause. In a study of primary and secondary amenorrheas, it was found that a differential diagnosis from the menopause could be made by the vaginal smear in about two-thirds of the case. If a smear showed marked atrophic changes in amenorrhea, any type of treatment for the condition was found to be useless. In studying the value of the vaginal smear in the diagnosis of carcinoma, cases that have been incompletely followed up and those in which tissues studies were not adequate have been discarded. In a group of 112 women in whom cancer was present or suspected, the smear diagnosis was incorrect in 11 cases; on the basis of comparison with a positive histologic diagnosis, the smear diagnosis was correct in 89 per cent. In 7 of the 11 incorrect smear diagnoses, the error was a false positive, and in only 4 a false negative and 2 of these 4 smears were reported as "suspicious." The vaginal smear technique is to be considered a definite addition to the diagnostic resources of gynecology. It is especially useful in the study of endocrine disorders in women and in the diagnosis of malignancy of the female genitals. Efforts should also be directed toward establishing a smear criterion of premalignant change.

COMMENT

The vaginal smear technic is definitely a very important addition to gynecologic diagnosis. It is particularly useful in the study of endocrine disorders and in the early diagnosis of cancer of the female genital tract. Never before have we had a diagnostic procedure for cancer in situ, the stage when absolute cure can be expected. Certainly this fact alone stamps this procedure as the most important diagnostic aid in cancer that has hitherto been proposed. It should be revolutionary. Every pathological laboratory must be equipped to perform these tests. ***H.B.M.***

Anaplastic Cervical Epithelium. Relationship to Cervical Carcinoma

C. T. Ashworth and A. W. Diddle (*Southern Medical Journal*, 41:217, March 1948) report that in a series of 1,815 specimens of cervical tissue obtained by biopsy and at hysterectomy, 16 showed non-invasive anaplastic epithelium, 6 early invasive and 293 frankly invasive carcinoma; the remaining 1,500 specimens showed no evidence of malignancy. The principal changes in the 16 specimens of non-invasive anaplastic epithelium were hypertrophy, hyperchromatism and variation in the size of nuclei. This epithelium also failed to differentiate as readily as normal epithelium. The basement membrane of this epithelium was intact but often disordered in contour, giving a lobulated effect. Histologically the anaplastic epithelium was similar to invasive carcinoma, except that it did not show invasion. Nuclear measurements showed that the nuclear volume curves were also similar in anaplastic epithelium and carcinomatous epithelium, differing strikingly from the normal in both types. The fundamental histologic identity of the cells of anaplastic epithelium and of invasive carcinoma of the cervix indicates that anaplastic cervical epithelium is essentially malignant. Several clinical studies have shown that patients

with anaplastic cervical epithelium may later develop invasive carcinoma of the cervix. Studies of experimental tumors have shown that the abnormal growth passes through several stages; and there is apparently an analogy between such stages in experimental carcinogenesis and anaplastic non-invasive epithelium and invasive carcinoma in the human cervix. In the authors' series one of every 3 women showing anaplastic epithelium in the cervix was under thirty years of age, while only one of every 36 women with clinical carcinoma of the cervix was in this early age group. These findings indicate that anaplastic epithelium of the cervix is malignant and is to be regarded as an early stage of cancer of the cervix.

COMMENT

In our zeal for the discovery of some means by which cancer may be discovered during its non-invasive stage several important facts have recently been brought to light. One of these is that anaplastic cervical epithelium has a definite relationship to invasive carcinoma of the cervix. In fact the authors believe that anaplastic epithelium of the cervix is malignant and is to be regarded as an early stage of cancer of the cervix. Another most important fact in this study was that 1 in very 3 women studied was under 30 years of age—the age group in which malignancy is most deadly. Such studies "put us ahead" in our ability to recognize cancer in situ, which really is early diagnosis. Complete ablation at this period of development is in fact "curative"; metastatic cancer is not curable. Every physician should become "cancer conscious" and utilize all the newer procedures for the early diagnosis of cervical cancer. ***H.B.M.***

A Multiple Sulfonamide Therapeutic Measure in the Postoperative Care of the Cervix and Vagina

A. H. Marbach (*American Journal of Obstetrics and Gynecology*, 55:511, March 1948) reports the use of a recently developed compound sulfa cream in the postoperative treatment following operations on the vagina and cervix. The sulfonamides in this cream are sulfathiazole, N-acetyl-sulfanilamide, N - benzoyl - sulfanilamide; urea peroxide is also a component of the cream. Laboratory studies have shown a high bacteriostatic and bactericidal action of this preparation at pH ranges of 4.6, 5.2 and 7.0. Within twenty-four hours after a vaginal or cervical operation or upon removal of the vaginal pack or cervical wick, approximately 5.0 Gm. of the cream was inserted into the vaginal canal twice a day. After the seventh postoperative day, patients were examined twice a week. In the 200 cases treated by this method, it was found that the malodorous discharge, usually a most annoying symptom after such operations, was reduced to a minimum and caused the patients no distress. Healing was definitely hastened as compared with results in similar cases in which the cream had not been used. In a series of cases in which conization of the cervix had been done healing was complete in sixteen to twenty-four days, as compared with twenty-eight to forty-two days, as reported by others. There was no postoperative occlusion of the cervical canal in these cases.

COMMENT

Vaginal antisepsis is always in order. It is not, however, very readily attained. On the other hand, there are certain germicidal agents that can be instilled into the vagina at regular intervals and a very high degree of positive action may be obtained. Apparently Dr. Marbach has done just this by a "multiple sulfonamide therapeutic measure." His results speak for themselves. Personally I have not used the author's technic but I can see no contraindication to its employment. Try it. Patients are always grateful for "no foul odors" and rapid healing which means home earlier. ***H.B.M.***

Current Reappraisal of Total Abdominal Hysterectomy

W. J. Reich and M. J. Nechtow (*American Journal of Surgery*, 75:670, May 1948) state that recent improvements in operative technique and in preoperative and postoperative care have resulted in a growing preference for total, rather than subtotal, abdominal hysterectomy. With total hysterectomy, not only is the danger of carcinoma in the cervical stump avoided, but also postoperative vaginal discharge due to endocervicitis, erosion, eversion or circulatory changes in the cervix following supracervical hysterectomy. Adequate preoperative care, including restoration of fluid and

electrolyte balance, and chemotherapy for the treatment of infection render the patient a better candidate for surgery. Either fluid or blood is given intravenously during the operation. During operation special care is taken to avoid injury to the ureters or to the bladder; the vaginal vault is supported posteriorly and anteriorly by a silk suture. If the adnexa are to be removed as well as the uterus, the salpingo-oophorectomy is done prior to the hysterectomy if possible; but in cases of pelvic inflammatory disease or endometriosis, it is often necessary to remove the uterus first. With the method of vaginal vault support now employed, no case of prolapse has been observed in the patients who have been followed up. Early ambulation is employed as a routine after total abdominal hysterectomy and penicillin is given every three hours for three or four days. Morbidity and mortality rates in the authors' series of total abdominal hysterectomy are about the same as those reported for subtotal hysterectomy.

COMMENT

The question of total vs. sub-hysterectomy will always be with us. However, with the recent improvement in preoperative preparation and diagnosis coupled with a better surgical tchnic it would seem that total hysterectomy should be the operation of choice. Naturally there will be a few cases where the surgical margin of safety is too narrow for any but the quickest operation the surgeon is capable of performing. When the cervix is left behind it should be thoroughly "coned" with the actual cautery, thus destroying the "main cancer-bearing area" of the cervix. The total operation has many other advantages in its favor but beware that the vagina is not shortened excessively. Unsatisfactory marital relations can cause "plenty trouble" and is a common cause of the "25-year divorce." It is a good plan to look into the sexual life of the couple before performing total hysterectomy. ***H.B.M.***

Army Seeks Civilian Doctors for Panama

Permanent appointments in the Civil Service, for physicians, now exist in the Panama Canal Medical Service, Major General Raymond W. Bliss, the Army Surgeon General, reports.

Salaries range from $5,599 to $7,794, with free transportation to the Canal Zone provided for physicians, their families and household goods. Return transportation is provided upon completion of a minimum of one year's service. In addition, doctors who receive appointments get two months paid vacation (including time lost by illness) and reduced fares on Panama Canal passenger vessels.

Physicians who desire experience in a tropical country under standard American living conditions may avail themselves of an unusual opportunity for broad general and tropical medical training in Central America.

Requirements for positions paying $5,599 to $6,540 are: Graduation from an approved medical school; license to practice medicine in a State; ability to pass a standard physical examination; completion of one year internship in a hospital approved by the American Medical Association.

Requirements for positions paying $6,540 to $7,794 are the same except that a minimum of three years of post-internship experience is required.

Medical officers accepted under the program will serve as physicians in out-patient treatment centers maintained by the Health Department of The Panama Canal in populous areas of the Canal Zone. All centers, whether large or small, are adequately staffed by graduate nurses and pharmacists.

Out-patient and dispensary service of The Panama Canal is backed up by world-famous Gorgas General Hospital and by a smaller general hospital at Colon. A hospital for the insane and indigent and a modern leper colony complete the hospital organizations of the Canal Zone.

Physicians who are interested in a position as medical officer in the Panama Canal Zone should communicate with Chief of Office, the Panama Canal, Washington, D. C. Applications also may be submitted to the U. S. Civil Service Commission, Washington, D. C.

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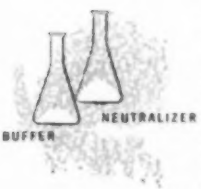

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1793 - 1864

Classical Quotations

● The patients have either suffered earlier from rheumatism or rheumatic symptoms appear at the same time, gently periodic sticking pains in the joints (in the ankles and in the knees, seldom in the hand and shoulder joint), which are oedematous, swollen and very painful when moved; the characteristic spots of the disease appear in the majority of cases first on the extremities and particularly on the lower ones (seldom on the upper ones), and here only up to the knee.

JOHANN LUKAS SCHÖNLEIN
Allgemeine und specielle Pathologie und Therapie, 1839, p. 42.

Medicine Tomorrow

Medicine Today, The March of Medicine, 1946. The New York Academy of Medicine Lectures to the Laity. New York, Columbia University Press, [c. 1947]. 8vo. 177 pages. Cloth, $2.00.

This volume contains the seven lectures to the lay public given under the sponsorship of the New York Academy of Medicine in 1946. Their purpose is to review some features of medical progress and to touch on the probably imminent changes in its practice.

All segments of our population should have access to the latest and best in medical practice. What such an ideal means from the point of view of the doctor, the individual and the Federal Government is the subject directly or indirectly of this series and is therefore worthy of study.

ANDREW BABEY

Dermatology

X-Rays and Radium in the Treatment of Diseases of the Skin. By George M. MacKee, M.D. & Anthony C. Cipollaro, M.D. Contributor, Hamilton Montgomery, M.D. 4th Edition. Philadelphia, Lea & Febiger, [c. 1946]. 8vo. 668 pages, illustrated. Cloth, $10.00.

The first part of the book is devoted to physics of X-Ray and Radium and is discussed in detail. The latter part is devoted to the treatment of the many skin diseases with recommendations of radiation therapy.

Throughout the book the authors do not hesitate to give the benefit of their experiences, both in clinic and in private practice. The text is simple and easily read. The book is profusely illustrated showing before and after therapy. Each chapter is followed by an extensive bibliography.

Medical students, general practitioners, and specialists will find it more than helpful in reference and application of the text.

GEORGE F. PRICE

Splenic Puncture

Die Milzpunktion. Technik, Diagnostische und Hamatologische Ergebnisse. By Sven Moeschlin, M.D. Basel, Switzerland, Benno Schwabe & Co., [c. 1947]. 8vo. 205 pages, illustrated. Cloth, 30 fr.

This book is the fruit of very intensive studies lasting over seven years on the puncture of the spleen. The author gives an excellent description of his type of needle, his technique and a list of the contraindications. Special attention has been given to comparing the spleen puncture findings with those of sternum and glands in cases of leukemia. The book is well written and offers a wealth of valuable information.

MAX G. BERLINER

—Continued on page 54

MEDICAL BOOK NEWS

—Continued from page 52

Socialized Medicine

Private Enterprise or Government in Medicine. By Louis Hopewell Bauer, M.D. Springfield, Ill., Charles C. Thomas, [c. 1948]. 8vo. 201 pages. Cloth, $5.00.

The reviewer has personally known the author of this book for many years as an outstanding physician in his community and as a man well qualified by virtue of his long experience in matters concerning the medical profession and the public welfare. He gives the reader plain facts in regard to the background of the problem, the deficiencies of our present system of medical care, the growth of government in medicine and public health, the comparison of compulsory sickness insurance in the various foreign countries and the details of recent, proposed legislation for compulsory sickness insurance in this country. He outlines the program of the American Medical Association and summarizes the ideals to be met and a ways of meeting them. Every doctor should read this book.

THOMAS B. WOOD

Blood

Morphologic Hematology. Special Issue No. 1 of BLOOD, The Journal of Hematology. William Damashek, M.D., Editor-in-Chief. New York, Grune & Stratton, [c. 1947]. 8vo, large. 200 pages, illustrated. Cloth, $4.75.

This volume is the first special issue of *Blood*. In its preface, William Dameshek, the Editor-in-Chief, emphasizes the great significance of morphology in this field, based largely on the recent development involving phase electron and fluorescence microscopy, as well as marrow culture methods, to mention a few.

The volume is given over largely to experimental studies. The article on bone marrow changes in active brucellosis and that on bone marrow changes in Hodgkin's disease are of immediate practical interest to the clinical pathologist.

Reports of this kind should serve to stimulate a well deserved and renewed interest in morphological changes in the blood.

THEO. J. CUPPHEY

Nutrition

Tomorrow's Food. The Coming Revolution in Nutrition. By James Rorty & N. Philip Norman, M.D. New York, Prentice-Hall, [c. 1947]. 12mo. 258 pages. Cloth, $3.50.

This meaty enlightening little volume covers in a nut-shell what is wrong with the American dietary, the evolution of these short-comings, and the ways and means for their correction. *Tomorrow's Food* should be a "must" on the reading list of every physician interested in nutrition. It breaks away from the provincial view-point of the practical nutritionist and delves into the field from the agronomist's angle. It is a startling portrayal of the rape of Nature via pressure politics.

GEORGE E. ANDERSON

Child Guidance

Psychiatry for the Pediatrician. By Hale F. Shirley, M.D. New York, Commonwealth Fund, [c. 1948]. 8vo. 442 pages. Cloth, $4.50.

This book does athoroug h job of integrating modern scientific trends in child guidance and psychology with the practice of pediatrics. Written ostensibly for pediatricians, the book will also be of interest to the psychiatrist, teacher, social worker, and nurse. A glossary of psychiatric terms is included for the convenience of the lay reader.

C. MILTON MEEKS

Eye Diseases

May's Manual of the Diseases of the Eye. For Students and General Practitioners. Revised and edited by Charles A. Perera, M.D. 19th Edition. Baltimore, Williams & Wilkins Co., [c. 1947]. 12mo. 521 pages, illustrated. Cloth, $4.00.

Doctor Perera carries on where Doctor May left off. Due to his close association with the late Doctor May in the preparation of the four previous editions, he has handled the work skillfully. Revisions and additions keep the book the gem former editions were. The section on ocular motility continues to be a handy quick refer ence for the busy specialist and an excellent introductory chapter to the novice in this field. Doctor Perera's revision very adequately meets the high standards of Doctor May.

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(MT-1)

LETTERS
TO THE EDITOR

REPRINTS

"I happen to have the degree of Master of Science (M.S) as well as the M.D. and my hobby-field is biophysics (in which field my M.S. was granted by Northwestern University, 1940). I maintain a private biophysical laboratory and I know what work and little sleep are! I am trying to say that I just simply CAN'T read everything that comes out in leading medical journals. I depend fairly heavily on your first-rate reprints for my information. To miss one would be a minor tragedy! When a pile collects, they are bound up in board covers and added to my library. Please *never* let me miss a reprint and please get *all possible reprints* to me; they mean a very, *very* great saving of time and effort."

R. W. Taraba, M. D.
Chicago, Ill.

"I wish to thank you for the reprint of the very important abstract which has recently been recieved. It made very enjoyable reading and will be of great value to all of us in this profession.

"I might add that I also enjoy reading your publication. Being a G. P. it has been of especial interest."

Leon S. Seidler, M. D.
Chicago, Ill.

LIKE MT

"Certainly enjoy reading your articles in MEDICAL TIMES and find them very practical and instructive."

John W. Fricke, M. D.
San Francisco, Calif.

"I read with great pleasure the article on 'Otitis Media' and I find this way of keeping the practitioner informed about the progress in various fields very useful."

Victor Mandler, M. D.
Bellmore, N. Y.

—Continued on page 46a

LETTERS

continued

ARTHRITIS

"Your summarization, 'Atrophic and Hypertrophic Arthritis,' is excellent and should be very useful to me.

"The one sentence on Bogolomets hardly covers the subject of ACS [antireticular cytotoxic serum]. I just returned from Mexico City; while there I learned that ACS was being rather widely used there and succesfully, too."

Henry D. Coles, M. D.
Chicago, Ill.

"I am glad to tell you that the articles are quite authoritative. For instance, I have compared your symposium on arthritis with the opinions expressed by authorities in this geographic area and find that your article is quite comprehensive and gives the evaluation of treatment, etc., as indicated here."

Gordon Mannerstedt, M. .D
Oakland, Calif.

SUMMARY ARTICLES

"I believe that this type of medical writing is going to prove very satisfactory."

Edwin C. Thorn, M.D.
Greenfield, Mass.

"I look forward to receiving your publication. The subject covered is usually timely, authoritative and complete. It is a method which is undoubtedly a time saver to the busy man."

Robert J. Armbrecht, M.D.
Wheeling, W. Va.

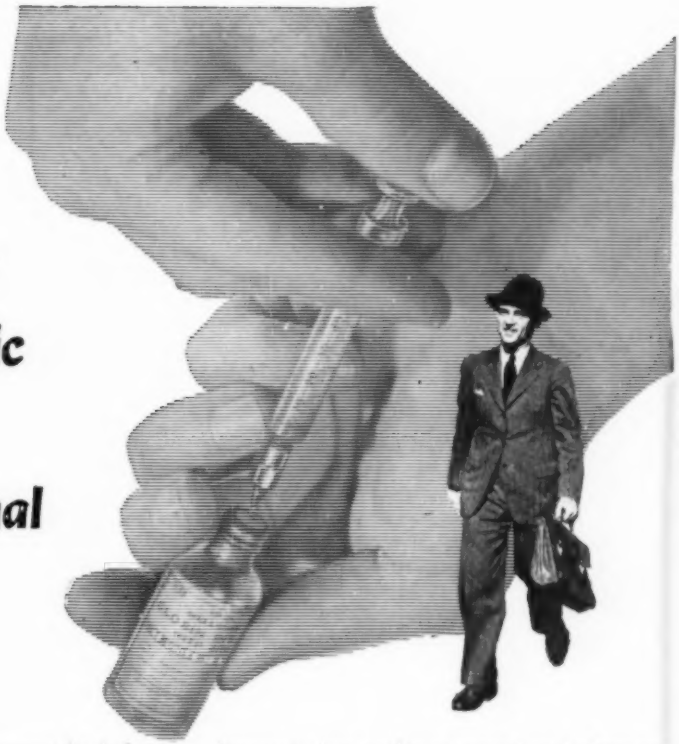
"Wonderful. Short, concise, condensed and to the point.

"Long articles tedious, and you generally lose interest or become too sleepy to get the punch line.

"Condensation, and down to earth scientific facts are usually retained, cerebrally speaking."

Arthur J. Burkel, M.D.
Buffalo, N. Y.

to convert the diabetic into a more normal person



"The ideal in therapy…is to convert the diabetic into a normal person."[1] While certain restrictions must always be imposed, many patients can be controlled through diet alone so as to dislocate their normal habits as little as possible. In those cases where insulin therapy is also required, control may often be attained with but *one daily injection* of 'Wellcome' Globin Insulin with Zinc. Its intermediate action is adaptable to the needs of most mild and many moderately severe cases and adequate control can usually be achieved in three clear-cut steps:

1. *Stabilize the patient* as well as possible on a diet of the desired caloric content. Give a single dose of 15 or 20 units of 'Wellcome' Globin Insulin 30 minutes or more before breakfast.

2. *Adjustment to 24-hour control:* Gradually adjust the Globin Insulin dosage to provide 24-hour control as evidenced by a fasting blood sugar level of less than 150 mgm. or sugar-free urine in the fasting sample.

3. *Adjustment of diet:* Simultaneously adjust the carbohydrate distribution of the diet to balance insulin activity. Initially this may be 2/10 (breakfast), 4/10 (lunch), and 4/10 (supper). Any tendency toward mid-afternoon hypoglycemia may usually be offset by giving 10 to 20 grams of carbohydrate between 3 and 4 p.m. The final adjustment of carbohydrate distribution may be based on fractional urinalyses.

Systematic attention to these details will make possible adequate control of most mild and many moderately severe cases of diabetes with a *single daily injection of 'Wellcome' Globin Insulin with Zinc.*

'Wellcome' Globin Insulin with Zinc is a clear solution, comparable to regular insulin in its freedom from allergenic properties. Available in 40 and 80 units per cc., vials of 10 cc. Accepted by the Council on Pharmacy and Chemistry, American Medical Association. Developed in The Wellcome Research Laboratories, Tuckahoe, New York. U.S. Patent No. 2,161,198. LITERATURE ON REQUEST.

'Wellcome' Trademark Registered

1. Bauman, L.: Bull. New Eng. M. Center 5:17 (Feb.) 1943.

'WELLCOME' Globin Insulin WITH ZINC

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Modern THERAPEUTICS

Hyaluronidase Increases Absorption of Fluids

Schwartzman, Henderson, and King, writing in *J. Pediat.* (33:267 (1948)), reported that they found the enzyme hyaluronidase to be of great value in increasing absorption of subcutaneously injected fluids, particularly in dehydrated infants. The extent and duration of pain and swelling usually associated with clysis of various solutions was greatly reduced by the use of the enzyme. Clysis could be given continuously for at least 5 days although the needle should be shifted after the third day. Sensitivity to the enzyme was found in 9.3 per cent of the cases given intradermal skin tests.

Vinbarbital Sodium in Obstetric Anesthesia

Vinbarbital sodium was given to 3,000 patients for analgesia and anesthesia during labor. Of the group, 556 received vinbarbital sodium only in average intravenous doses of 15 gr. The remaining 2,444 were given 9 gr. orally along with 1/150 gr. of scopolamine, and occasionally the barbiturate was given intravenously for the completion of delivery. Lewis and Boddie state in *South. Med. J.* (41:820 (Sept. 1948)), that labor was not retarded and there were no serious fetal or maternal complications traceable to the vinbarbital. There were 2,978 infants born alive altogether, of which 80.8 per cent breathed spontaneously, 12.6 per cent were slightly asphyxiated, while 6.3 per cent required drastic measures to start breathing. There was apparently no relationship between the amount of vinbarbital given the mother and the degree of asphyxia in the infant.

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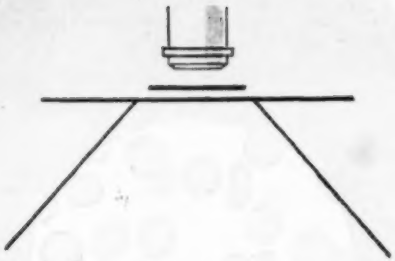

The Blood Picture Responds More Quickly

While iron is essential for hemopoiesis, recent findings give evidence of the important role in blood formation played by B-complex vitamins and certain factors occurring in fresh liver concentrate. This approach may be considered as "Supported Therapy," from which rapid correction of both the blood picture and the systemic manifestations of anemia may be expected.

Livitamin with Iron is indicated in hypochromic anemias regardless of origin and routinely during pregnancy and lactation. Its liquid form and palatable taste make it especially valuable for administration to children. Adult dose, 3 to 4 teaspoonfuls 3 times daily.

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Each fluidounce of Livitamin with Iron, prepared with an attractive, palatable vehicle, presents:

Iron and Manganese Peptonized..30 gr.
(Equiv. to 45 mg. elementary Iron)

Iron Peptonized, N.F.....12½ gr.
(Equiv. to 140 mg. elementary Iron)

Thiamine Hydrochloride (B_1)..10 mg.

Riboflavin (B_2, G).....5 mg.

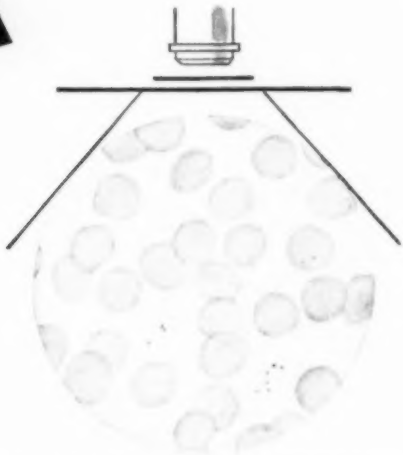
Nicotinamide (Niacinamide)...25 mg.

Pyridoxine Hydrochloride (B_6)..1 mg.

Pantothenic Acid.....5 mg.

Liver Concentrate 1:20.....45 gr.
(Represents 2 oz. fresh liver)

Rice Bran Extract.....15 gr.



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SEMCO

—Continued from page 48a

Experimental Tuberculosis Treated With Sulphetrone

Bovine tubercle bacilli were recovered from 19 of 20 guinea pigs treated with Sulphetrone (tetrasodium 1,1'-(sulfonyl bis (p- phenylene - imino)) - bis(3 - phenyl-1,3-propanedisulfonate) but the average survival time was 77 days as compared with 45 days for the untreated group. According to Brownlee and Kennedy in *Brit. J. Pharmacol. Chemotherap)* (3:29 (1948)) the treated group received an average of 0.6 Gm. of the drug a day for the first fifteen days after infection. Another group of guinea pigs were infected with a culture of human strain tubercle bacilli. All of the 21 untreated animals were dead within 154 days after infection but only 6 of 24 similarly infected animals were dead in the same time period when they were treated with Sulphetrone. The authors also state that the extent of development and the severity of the disease was much less in the treated group. From these experiments the authors concluded that the drug is bacteriostatic but that it is not bactericidal to the tubercle bacilli.

Propylene Glycol as Vehicle for Sulfathiazole

A 3 per cent solution of sulfathiazole in propylene glycol proved to be an effective vehicle in a number of otolaryngologic conditions. Blackford, writing in *Laryngoscope* (58:336 (1948)), claimed that the 94 patients treated with this solution generally recovered more rapidly and with clearer postoperative fields than did those not treated. The patients receiving treatment for nasal or auditory canal infections were quickly relieved of pain. No untoward reactions were noted. The solution was not effective in the treatment of chronic eczema of the external auditory canal, mycotic in-

—Continued on page 52a

—Continued from page 50a

fections of the ear, or furunculosis of the external auditory canal.

Role of Sulfadiazine in Hyperthyroidism

In an effort to prevent postoperative infections following thyroidectomy Mulholland, Lawler, and Ralli gave 8 Gm. of sulfadiazine orally in divided doses the day before operation. The drug was also continued in doses of 4 Gm. a day for 2 to 4 days following the operation. The authors report in *Surg. Gynecol. Obstet.* (86:413 (1948)) that in the 75 patients so treated there was no severe postoperative reaction and the temperature and pulse rate were well controlled. Evidence pointed to an antithyroid as well as an anti-infective effect. Thus, in patients who had not received sulfadiazine preoperatively and who showed signs of thyroid crisis after operation, such as rapid heart rate, restlessness, and a rise in temperature to 101° F., the drug was given. Within 12 hours, in every instance, the temperature and heart rate decreased and the patient's condition improved.

Vitamin K in Treatment of Chilblains

Vitamin K appears to offer definite promise in the treatment of chilblains. According to Wheatley in *Brit. Med. J.* (#4530:689 (Nov. 1, 1947)) 4 of 8 cases treated were completely relieved of symptoms and the other 4 were improved. The cases of chilblains ranged from the mildest to ulcerated forms. The predisposing factors in chilblains are assumed to be defective peripheral circulation with increased permeability of the vessel walls and diminished coagulability of the blood. These same abnormalities are present in vitamin K avitaminosis. The dosage and duration of therapy varied from person to person. An average oral dose of 20 mg. twice a day was found to be most satisfactory. Intramuscular injections were superior but too painful.

—Continued on page 54a

RIB-BACK BLADES

afford an excellent example as they are built up to a quality —not down to a price. Although their initial cost is slightly more per dozen, a cost analysis over a given period will often reveal that their comparative cost is actually less per individual blade.

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MODERN THERAPEUTICS

—Continued from page 52a

Phenosulfazole Halts Mouse Poliomyelitis

A sulfonamide informally known as phenosulfazole, chemically *n*-(2-thiazolyl)-phenosulfonamide, has shown great promise in the treatment of poliomyelitis in mice. The results obtained were: a cure of mice in the early stages of the disease, immunity to reinfection among those which survived, and the prevention of reinfection. Hultquist, Parker, and associates found that the new sulfonamide protected mice given as much as 100 times the lethal dose of poliomyelitis virus even when administered as much as 24 hours after the virus was given. Mice in the control group failed to survive much smaller doses of the virus. In the report in *Chem. Eng. News* (26:2710 (Sept. 13, 1948)) it was stated that the virus followed a normal deterioration curve when placed in a cell-free serum with the drug. However, when the drug was placed in embryonic mouse brain culture infected with the virus, the growth of the virus was halted abruptly. Thus, it appears that the drug acts on the tissue cell itself rather than directly on the virus. Phenosulfazole is apparently entirely lacking in toxicity for mice and monkeys. A preliminary study in the use of this sulfonamide in human beings has been started.

Effects of Intravenous Injection of Tetraethyl Ammonium Chloride

Within 39 seconds after the injection of 5.5 to 7.7 mg. of tetraethylammonium chloride per Kg. of body weight in 8 subjects there was a statistically significant decrease of the intra-arterial systolic blood pressure and an increase in heart rate. There was also an increase in the volume of the leg and ear and a decrease in gastrointestinal motility. According to Brown, Wood and Lumbert in *J. Pharmacol.* (93: 10 (May, 1948)) the effect on the motility of the rectum lasted as long as 72 minutes while the effect on the arterial pressure and the heart rate lasted for 20 to 25 minutes.

—Continued on page 56a

WINTER *and* PSORIASIS

Dermatologists have observed that lack of sunlight aggravates the lesions of psoriasis. This may account for patches appearing on the parts which are covered with clothing and hair.

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RIASOL contains 0.45% mercury chemically combined with soaps, 0.5% phenol and 0.75% cresol in a washable, non-staining, odorless vehicle.

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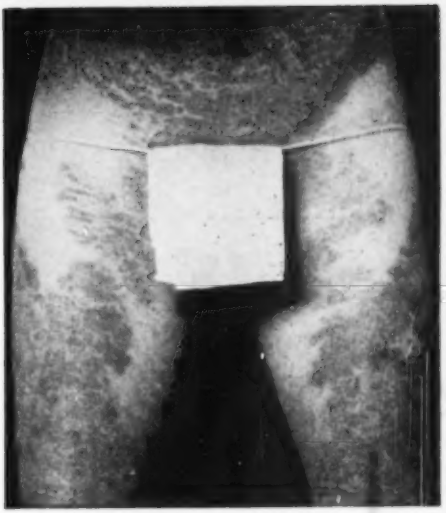

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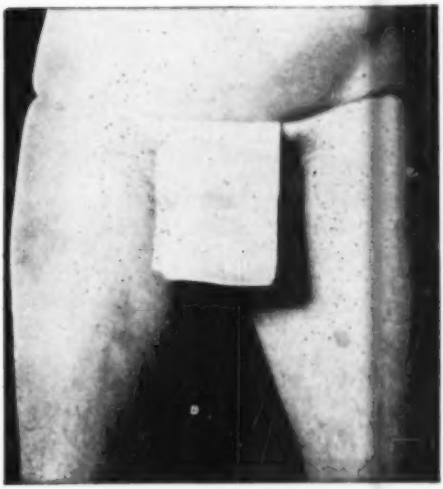

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RIASOL for PSORIASIS

—Continued from page 54a

Reduction of Dental Caries with Topical Sodium Fluoride

Further studies relative to the reduction in the incidence of dental caries reveals that a 1 per cent solution of sodium fluoride is apparently as effective as the usual 2 per cent solution. Writing in *Pub. Health Reports* (63:1215 (Sept. 17, 1948)) Galagan and Knutson report the results obtained from studies of several series of patients in whom diagonal quadrants of their teeth were treated and the opposite quadrants were untreated as controls. They also investigated the possibility that application of a 5 per cent solution of calcium chloride immediately following the application of sodium fluoride would cause the deposition of calcium fluoride. It was hoped that this would increase the effectiveness of the treatment. However, no significant difference was noted between the comparative series. The authors found that an increase in the time interval between treatments from one or two weekly at the beginning of the observation year to one treatment every 3 or 6 months decreased the caries-inhibiting action. They also feel that at least 4 treatments are necessary to obtain full effectiveness, with an initial cleansing of the teeth. The application of the sodium fluoride solution by means of a fine spray was as effective as the usual cotton applicator.

Repository Penicillin Therapy

An injectable vehicle for penicillin which is fluid at ordinary room temperature, does not require special syringes for injection, does not cause local reaction, and which is equal or superior to the wax-oil or similar vehicles has been the subject of

—Continued on page 58a

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study by many workers. Ercoli and associates proposed a preparation composed of crystalline potassium penicillin, 300,000 units; epinephrine, 0.3 mg.; and vegetable oil, 1 cc. Writing in *J.A.M.A.* (136:115 (Sept. 11, 1948)) the authors reported that the preparation produces effective blood levels of penicillin after 300,000 or more units are given for periods from 15 to 24 hours. The preparation was given intramuscularly or subcutaneously. The later method of administration produced the longest blood levels. In no case was there a significant increase of blood pressure which could be attributed to the epinephrine.

Thiamine Hydrochloride Potentiated for Herpes Zoster

The action of thiamine hydrochloride in the treatment of herpes zoster has been explained by Waldman and Pelner on the basis of its inhibition of cholinesterase, with the resultant liberation of more acetylcholine. This is essentially the same action as neostigmine. Thus the authors reported in *N. Y. St. J. Med.* (47:1997 (Sept 15, 1947)) on the combined use of these two drugs in 23 cases of idiopathic herpes zoster. The results were impressive. When diagnosis was definitely established 1 cc. (100 mg.) of vitamin B_1 and 1 cc. (1:2000) of neostigmine methyl sulfate were given intramuscularly in the same syringe. This dose was repeated on alternate days until pain was relieved. The number of injections required varied with the age of the patient and the duration of symptoms.

Calciferol In Treatment of Cutaneous Tuberculosis

Oral treatment with calciferol (vitamin D_2) in 12 patients with cutaneous tuberculosis resulted in the cure of 6 and improvement in 5 of the others. Three 50,000 unit

—Continued on page 60a

MODERN THERAPEUTICS

—*Continued from page 58a*

tablets were given each day or two 600,000 unit doses of an alcoholic or an oil solution were given each week. An ointment containing 70 units per Gm. was applied locally to the resistant cases and the lesions showed improvement. However, when an ointment containing 150,000 units per Gm. was applied the lesions returned to their original state. Toxic effects including salty taste in the mouth, thirst, anorexia, nausea, abdominal pain, lassitude, and micturition occurred in most of the patients. Since experiments showed that *in vitro* concentrations of calciferol as high as 500 units per cc. had no effect on *Mycobacterium tuberculosis*, Powell, Pearsall, and Wigley, writing in *Brit. Med. J.* (1:386 (Feb. 28, 1948)) concluded that it seemed probable that calciferol acted *in vivo* by increasing body resistance to the bacteria.

Streptomycin in Ocular Infections

Bellows and Farmer conclude that there is definite evidence that in most cases of acute and chronic infections of the conjunctiva and cornea organisms are rapidly eliminated by streptomycin therapy. The authors base their conclusion on 23 clinical cases and upon experimental studies reported in *J. A. M. A.* (135:491 (Oct. 25, 1947)). Relapses occur if therapy is discontinued too soon. The general procedure for patients was to administer drops containing 10,000 micrograms of streptomycin per cc. at one hour intervals during the waking hours. This regimen was continued for 8 days. The antibiotic was found to be safe and nonirritating to the surface of the eyeball in concentrations up to 10,000 micrograms per cc. of isotonic sodium chloride solution. For infections of the vitreous, solutions containing 500 micrograms in 0.1 cc. of isotonic saline are injected.

Stability of Penicillin in Lozenges

The lozenges were obtained from routine manufacturing batches and were stored in closed screw-capped jars. Storage was at

room temperature. The base used in the preparation of the lozenges was composed of equal parts lactose and sucrose, with a suitable amount of powdered tragacanth. The mass was granulated with the addition of mucilage of tragacanth. The calcium penicillin was dispersed in dry sterile magnesium stearate. Additional magnesium stearate was used as the lubricant. The finished lozenges weighed 1 Gm. and contained either 500 or 1000 units of penicillin. Barnard and Hartley stated that the lozenges were assayed by the cup-plate method at intervals up to one year. No significant loss in activity was observed. During the discussion it was pointed out that the use of silica gel with anhydrous cobalt chloride gave a false sense of security as to the stability of the lozenges in the container holding these substances. The cobalt chloride was supposed to show a color change indicating that sufficient water had been absorbed by the lozenges and gel to suggest deterioration of the lozenges. However, it was pointed out, in *Pharm. J.* (*161*:160 (Sept. 4, 1948)) that the author had added water to such a container and the lozenges took up the water but there was no change at all in the anhydrous cobalt chloride.

Preliminary Observations on Aureomycin

Aureomycin is a new antibiotic derived from a strain of *Streptomyces aureofaciens*. It is supplied as a yellow crystalline hydrochloride, soluble in distilled water but less soluble in isotonic sodium chloride solution. Its solutions are acid in pH. In alkaline solutions the antibiotic activity deteriorates rapidly. The LD_{50} upon injection subcutaneously in mice is between 3,000 and 4,000 mg. per Kg. of body weight. Autopsy following repeated large doses in rats and dogs showed no grass or microscopic abnormality. Writing in *J.A.M.A.*

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(*138*:117 (Sept. 11, 1948)) Bryer *et al* stated that a 1 per cent solution of aureomycin borate was tolerated in the eye of a rabbit. Serum concentrations obtained ranged from 0.3 to 2.4 micrograms per cc. No antibiotic was detected in the spinal fluid but high concentrations were found in the urine. The antibiotic does not seem to be as effective when given orally. Clinically aureomycin showed favorable initial responses in cases of Rocky Mountain spotted fever, *Escherichia coli* infections of the urinary tract, brucellosis and typhoid.

Clinical Value of Pregnandiol Assays

A modification of the Guterman technique for the assay of pregnandiol is described by Swyer in *Proc. Soc. Endocrinol.* through *J. Endocrinol.* (*5*:87 (1948)). Photo-electric colorimetry is used to give quantitative results. This technique is not highly accurate but it is sufficiently so for routine clinical use as a test for pregnancy and as a prognostic aid in threatened abortion. The highest value obtained in a study of 28 non-pregnant women was 5 mg. of pregnandiol per liter of urine. Thus, an excretion of more than 6 mg. per liter was considered indicative of pregnancy. Upon

this basis the assays compared well with Friedman tests performed on the same patients. Since there is day to day variation in the excretion of pregnandiol it was felt that more than one assay is necessary. In 5 cases of threatened abortion in which the pregnancy continued the pregnandiol assay gave results of from 16 to 28 mg. per liter, while in 3 cases in which abortion became complete the assay gave results of from 0 to 5 mg. per liter.

Subcutaneous Administration of Sulfonamides in Children

According to Slobody, Lehr, and Willner in *Pediatrics* (2:58 (July 1948)) the administration of a combination of sulfadiazine and sulfamerazine subcutaneously to 60 children under 5 years of age resulted in well-sustained blood levels and good therapeutic responses. The drugs were given as a 2.5 per cent solution (each) in

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MODERN THERAPEUTICS

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doses of 0.065 Gm. per Kg. of body weight every 12 hours. As much as 0.1 Gm. per Kg. was given for a few days in severe cases. Good results were obtained in such infections as influenzal meningitis, bronchopneumonia, otitis media, follicular tonsilitis, enteritis and spesis of the newborn. Maximum blood levels were reached within 2 hours after administration. Transient crystalluria occurred in 5 patients and no local reactions developed. A combination of sulfadiazine and sulfathiazole produced local irritation and did not give comparable blood levels.

Painless Labor with Intraspinal Nupercaine

Perineal anesthesia occurred in 5 to 10 minutes and lasted 2 to 4 hours following injections of Nupercaine (2-butoxy-N-(beta-diethyl-aminoethyl) cinchoninamide) in glucose. Relief from uterine constrictions lasted for 1 to 2 hours and developed within 1 to 4 minutes following the injection. One injection should be sufficient if properly timed but more than one injection does not seem to be contraindicated. About 200 cases were administered the anesthetic, in which the most serious side reaction was headache. Berlowe and Herrick, writing in *Connecticut Med. J.* (12:417 (May

1948)), stated that in 100 patients in whom the injection was given into the 2nd lumbar interspace 96 per cent received complete relief, but when the injection was given into the 4th lumbar interspace only 79 per cent of 100 patients received complete relief.

Pharmacology and Chemotherapy of Sulphetrone

Studies with mice and dogs indicated that Sulphetrone (4,4'-bis(-phenyl-n-propyl-amino) diphenylsulfone tetrasodium sulfonate was practically non-toxic when given over short periods of time. Studies with rabbits indicated that its chronic toxicity is low. In *Brit. J. Pharmacol.* (3:15 (1948)) Brownlee, Green and Woodbine state that the drug is slowly absorbed from the intestinal tract. There is no conjugation of the drug in the body. It penetrates all tissues quite rapidly, with the exception of the brain, and in the cerebrospinal fluid the penetration is slow. The drug was found to be active *in vitro* against 3 strains of *Mycobacterium tuberculosis* var. hominis as well as non-human strains. It was also effective against *beta*-hemolytic streptococcus infections in mice but was not effective against pneumococcus infections. The authors suggest that this drug has value in the treatment of experimental tuberculosis and its use in human subjects seems to be practically possible.

Dental Points Impregnated With Penicillin

One treatment sterilized the cultures of 33 of 44 persons requiring root canal therapy, all of whom showed periapical infections. Treatment consisted of use of a rubber dam, iodinizing the field, cleansing

—*Continued on page 66a*

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the root canal, washing with penicillin concentrate solution, and cement-sealing in the canal a cotton point impregnated with 3,000 units of crystalline penicillin sodium, dry or slightly moistened. Buchbinder and Schwartz discuss this treatment in *J. Dental Research* (27:211 (Apr. 1948)) and state that sterilization occurred in an average of 1.9 visits. Points which were extracted in a 1 per cent phosphate buffer solution having a pH of 6.0 twenty four hours after being placed in the root canal, assayed against *Staphylococcus aureus* as having an activity corresponding to 50 units of penicillin. After 48 hours the activity corresponded to about 8 units. *Streptococcus viridans, Staphylococcus albus,* and *Staphylococcus aureus* were the most common bacteria found in the cultures from root canals.

Bacitracin and Penicillin in Rabbit Syphilis

Experimental trial in rabbits with syphilis revealed that the intramuscular administration of 2,300 units of bacitracin per Kg. of body weight once a day for 4 days cured half of the rabbits tested. Writing in *Proc. Soc. Expt. Biol. Med.* (68:415 (June 1948)) Eagle and Fleischman revealed that bacitracin and penicillin were synergistic when given together. One mg. of penicillin per Kg., which is about 1/40 the CD_{50} (dose curing half the animals), when given concomitantly with 1,280 units of bacitracin per Kg., which is about 1/7 the CD_{50}, was found to be curative.

MEDICAL (advertisers index) TIMES
JANUARY, 1949

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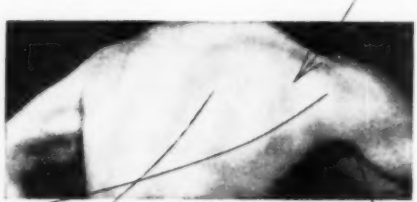

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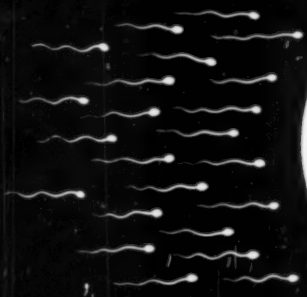

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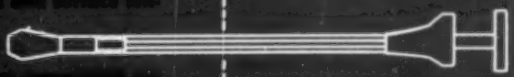

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**Reich, Button and Nechtow, "Treatment of Trichomonas Vaginalis Vaginitis," Surgery, Gynecology and Obstetrics, May 1947, pp. 891-896*

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